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THE ORIGIN OF HISTIOCYTES (MACROPHAGES) IN THE LUNGS

AN EXPERIMENTAL STUDY BY THE USE OF INTRATRACHEAL INJECTIONS OF VITAL STAIN *

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The protective mechanism of the lungs against infection with bacteria, or foreign particles which had made their way directly into these structures, was an object for investigation by the earliest bacteriologists and hygienists. In 1876 von Ins [1] had already noted large cells studded with particles in the pulmonary alveoli, which he first designated as *"Staubzellen"*—"dust cells."

The literature of the last twenty-five years of the nineteenth century abounds with reports concerning the "permeability" of the epithelial cells lining the pulmonary alveoli. Two questions have aroused the particular interest of investigators: (1) the precise nature of the cells lining the alveoli, and (2) the source of the large epithelioid cells found in the alveoli during certain inflammatory and congestive processes such as tuberculosis.

Experiments with the intratracheal insufflation of soot, indigo and pulverized charcoal, and also with the intratracheal injection of bacteria, have led observers to different conceptions: either, (1) that the large phagocytic cells found in the pulmonary alveoli originate from the epithelial cells lining the alveoli; or (2) that they originate from hematogenous elements, namely, from leukocytes.

Among recent experiments those of Briscoe [2] are of interest. His procedure was to inject intratracheally in laboratory animals physiologic sodium chloride solution, pigeons' red corpuscles and *Bacillus mesenteri-*

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1. Von Ins: Experimentelle Untersuchungen über Kiesselstaub Inhalation, Virchows Arch. f. path. Anat. **73**:151, 1878.

2. Briscoe, J. C.: An Experimental Investigation of the Phagocytic Action of Alveolar Cells of the Lungs, J. Path. & Bact. **12**:66, 1908.

cus vulgaris. The animals were killed at different intervals, from thirty minutes to seventy-five hours after injection, and the tissues were fixed in the usual manner. His conclusions were that the phagocytic cells of the lungs are an essential part of the alveolar lining, and that these cells are probably derived from the epithelial elements.

To trace the genesis of a particular type of cell in fixed tissues (pathologic or normal) is extremely difficult. A differentiation of cells based on morphologic characteristics only is unreliable. Moreover, phagocytes being migrating cells, attracted by chemical substances of a different nature or by bacteria, frequently assume various aspects dependent on a variety of conditions. The solution of the problem by the use of old procedures was therefore not possible.

Methods of intravital staining recently introduced in experimental pathology held greater promise. Goldmann's [3] experiments made it known that there is a system of cells scattered all over the body that possess a common affinity for vital dyes (pyrrol blue, trypan blue, etc.) which become stored in the cytoplasm in the form of droplets of various size. The blood cells, the elements of lymphoid or myelogenous origin, as well as other cells of the parenchyma, remain unstained.

By the use of intravital staining, then, one is able to recognize a special variety of cells which in the earliest stages of ontogenesis are derived from the embryonic connective tissue, the mesenchym. These cells include the clasmatocytes of Ranvier found in the loose connective tissue, the adventitial cells of Marchand, the pyrrol cells of Goldmann, the polyblasts of Maximow, the reticular cells and the cells of the sinuses in the lymph nodes, in the spleen and bone marrow, and finally the Kupffer cells in the liver. Close investigation has shown that the large phagocytic cells described previously by Metchnikoff under the name of macrophages, because of their outstanding phagocytic activities, belong in the same category. Consequently, from the physiologic standpoint, this group of cells has been considered to have in common two essential characteristics, namely phagocytosis and storage of vital dyes. Aschoff and Kiyono [4] have designated these cells as "histiocytes" (tissue cells), and on the basis of their common physiologic characteristics have grouped them together under the name of the reticulo-endothelial system.

Sewell [5] was the first to apply the method of vital staining for the study of the origin of phagocytic cells in the lungs. His experiments

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3. Goldmann, E. E.: Die äusere and innere Secretion des gesunden und kranken Organismus im Lichte der vitalen Färbung, Beitr. z. klin. Chir. **64**:192, 1909; **78**:1, 1912.

4. Aschoff, L.: Das Reticulo-Endotheliale System, Ergebn. d. inn. Med. u. Kinderh. **26**:1, 1924.

5. Sewell, W. T.: The Phagocytic Properties of the Alveolar Cells of the Lungs, J. Path. & Bact. **22**:40, 1918-1919.

can be divided into two groups: (1) intravenous injections of a solution of lithium carmine followed by the intratracheal injection of Chinese ink, pigeon's blood and *Staphylococcus pyogenes aureus,* and spores of oidium albicans; (2) intratracheal injection of solutions of lithium carmine and trypan blue, respectively, in normal guinea-pigs. As a result of his experiments he states that the lungs are poorly supplied with fixed histiocytes. He believes, however, that the alveoli of the lungs are "provided with a highly specialized system or tissue of phagocytic cells, independent of the wandering macrophages, and that these cells play a very important and active part in the early stages of inflammatory conditions in the alveoli."

More recently Westhues,[6] from Aschoff's laboratory, approached the problem in a similar way. Guinea-pigs were given a single injection of carmine, subcutaneously or intratracheally, and were killed shortly afterward. Westhues concluded from his studies of the tissues that "the phagocytic cells found in the pulmonary alveoli do not originate from the alveolar epithelium." Experiments reported by Foot,[7] and by Permar [8] are to the effect that the large phagocytic alveolar cells are derived from the capillary endothelium of the alveolar septums.

In view of the lack of agreement on the part of these several authors I was prompted to investigate the problem anew.

MATERIAL AND METHODS

A sterile solution of 1 per cent of pyrrol blue (National Medicinal Products) in Ringer's fluid, filtered through a thin layer of sterile cotton, was used in all experiments. This was injected intratracheally into rabbits and guinea-pigs, respectively, intravenously into rabbits and intraperitoneally into guinea-pigs and white rats. Previous to the injection the dye was always heated at 37.5 C. to bring it as close as possible to the body temperature. The intratracheal injection was made by inserting a needle between the lower rings of the exposed trachea, according to a method previously described.[9]

Tissues which were fixed in 10 per cent formaldehyde were studied in paraffin sections, stained with hematoxylin and eosin, and also on frozen sections.

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6. Westhues, H.: Herkunf der Phagocyten in der Lunge, Beitr. z. path. Anat. u. z. allg. Pathol. **70**:221, 1922.

7. Foot, N. C.: Studies on Endothelial Reactions, J. Exper. Med. **32**:513 and 533, 1920; **33**:271, 1921.

8. Permar, H. H.: The Mononuclear Phagocytes in Experimental Pneumonia, J. M. Research **44**:27, 1923.

9. Fried, B. M.: The Appearance of Specific Antibodies in the Serum of Rabbits by Intratracheal and Intravenous Injections of Living Tubercle Bacilli, Proc. Soc. Exper. Biol. & Med. **21**:396, 1924.

EXPERIMENTS

I. *Intraperitoneal Injection of Pyrrol Blue.*—The albino rat and the guinea-pig were used in this series of experiments. Three cubic centimeters of the solution was injected intraperitoneally at one time, the number of injections varying from one to six. When several injections were made, the interval between the injections was twenty-four hours. The animals in all instances were killed about twenty-four hours following the last injection.

Results.—The skin and the viscera of the animals were markedly blue, the intensity of the color being variable, depending on the number of injections. The abdominal organs, particularly the liver and omentum, were deeply stained.

Microscopically, the liver and spleen showed the usual characteristic staining of the histiocytes (reticular cells and the endothelial cells of the sinuses in the spleen, and Kupffer cells in the liver). The lungs, as compared with the abdominal viscera, were poorly stained. Microscopically, the dye in these organs was found only in the intima and media of the larger vessels, and occasionally in the circular muscular layer of the bronchi. A few histiocytes scattered here and there around the vessels, as well as in the alveolar septums, had taken up the dye. The histologic structure of the lungs appeared normal.

II. *Intravenous Injections of Pyrrol Blue.*—This series of experiments was conducted on rabbits. Five cubic centimeters of the solution was injected daily into the marginal vein of the ear with an interval of twenty-four hours. The animals were killed twelve hours after the last injection.

Results.—In this series of experiments as in the foregoing, the repeatedly injected dye, while literally "soaking" the viscera, pelvic organs and genitalia of the animals, had stained the lungs to a slight degree only.

The cells of the histiocytic group were abundantly stained in the liver, spleen and other abdominal viscera. In the lungs the dye was stored often in the adventitial cells of the larger vessels, faintly in the vascular intima and media (apparently because of the permeability of the vessel wall), and here and there in large cells seen in the interalveolar septums, which, judging from the morphology and also from the fashion in which the dye is distributed in cellular cytoplasms, are histiocytes. The other pulmonary structures were untouched by the stain. The lungs did not show any histologic changes.

Comment.—Both Sewell and Westhues in their experiments with intravenous injections of a vital stain for the purpose of investigating the genesis of the macrophages of the lungs had observed that the cells of the histiocytic group were few.

Goldmann,[8] who had been impressed by the scantiness of the dye in the lungs of animals vitally stained by intravenous or intraperitoneal injections, assumed that the liver had taken up the bulk of the dye which consequently reached the lungs in an insignificant amount.

It would appear that the scantiness with which the pulmonary tissue is stained when the dye has been introduced by way of the veins or

Fig. 1.—A pulmonary alveolus from a rabbit intravitally stained by repeated intratracheal injections of pyrrol blue. The alveolar wall is thickened; individual cells are greatly enlarged; a few cells have taken up the dye in a characteristic histiocytic manner. In the center is a "dust cell" also typically stained.

peritoneum may be due to a number of factors. 1. The Kupffer cells of the liver retain the dye and thus act as a barricade, in which the polygonal hepatic cells themselves also play some rôle though a non-specific one. 2. The dye becomes greatly diluted when given by intravenous or intraperitoneal injections. 3. A large part of the injected material is excreted by the urine and feces, and Goldmann [3] demonstrated the presence of trypan blue in the bile of his animals.

It was thought, consequently, that an insufficient amount of the dye had reached the lungs to call forth the histiocytes, and to conclude from the foregoing experiments that the lungs are actually poor in histiocytes seemed premature. Accordingly, it was determined to inject the dye *intratracheally*, and to study the effects of its direct application to the lung.

III. *Intratracheal Injection of Pyrrol Blue.*—The series of experiments was conducted on rabbits and guinea-pigs. The experiments were of two types: (1) A single intratracheal injection ("acute" staining) was made and the animals were killed at varied intervals following the injections; (2) repeated ("chronic" staining) intratracheal injections were made.

1. *"Acute" Intratracheal Staining of Animals.*—Two cubic centimeters of 1 per cent of pyrrol blue was injected into the trachea of guinea-pigs, and 5 cc. into the trachea of rabbits, respectively. The injections caused the animals no apparent discomfort. The animals of the series were killed at intervals of from one-half hour to seventy-two hours subsequently.

Results: Gross Description of the Lungs.—The dye, no matter how soon after injection the animal was killed, was usually found to be more abundant around the hilum and along the posterior aspect of the lungs, where the organs were uniformly and deeply stained. In the lower lobes and also at the apexes it was conspicuous as pin-point spots. The heavily stained portions of the lungs seemed to be expanded and the overlying pleura appeared to be smooth and tense, whereas in the unstained areas it had its usual wrinkled appearance. Fresh sections of the lungs showed the distribution of the dye to correspond with that on the external surface, namely a diffuse stain in certain areas and a punctate staining in others.

Microscopic Examination.—Tissue was taken from different parts of the lungs. Paraffin as well as frozen sections were studied.

The striking feature in the sections was the fact that the dye did not appear to be uniformly distributed even in the areas where grossly the tissue was uniformly and deeply stained; for even in these areas it was found to be scattered in patches. These patches were composed of clumps of large cells having an oval or irregularly round nucleus and a large amount of cytoplasm which had stored the dye. The distribution of the dye in these cells was characteristic in that it was deposited as coarse and fine droplets all through the cytoplasm leaving the nuclei unaffected. In brief, these cells were morphologically identical with the large phagocytic cells (dust cells) found in the alveoli. The manner in which they had stored the dye showed them to be typical histiocytes (fig. 1).

Besides the "tatooed" cells found in the alveoli, numerous cells which had taken up the dye in a similar manner were "adherent" to the alveolar wall. These

cells were unmistakably the so-called alveolar epithelial cells which projected into the pulmonary alveolus in a budlike manner. Frequently, under high magnification, they could be seen to be partly detached from the alveolar wall. They were usually enlarged, showing occasionally a foamy cytoplasm. Their close resemblance to the cells lying free in the alveolus was morphologically striking. By the manner in which they had taken up the vital stain it is evident that both cells belong to the same strain (fig. 1).

In the heavily stained areas the cells lining the alveoli appeared somewhat swollen, with occasional vacuolization of their cytoplasm. In places they showed such marked proliferation as to form microscopic areas of solidification with the obliteration of the normal alveolar structure.

The remainder of the pulmonary tissue was normal. The dye was found in the subepithelial layer of the bronchi whose epithelium showed no changes. It was also present in the intima and media of the vessels which appeared like bands of blue ribbon. The endothelium of the capillaries, as well as of the larger vessels, showed no proliferative changes.

Comment.—In this series of experiments the following points are of interest. Though the dye was injected by way of the trachea directly into the lungs, only an insignificant portion of these organs was affected. In those areas where the dye was concentrated there was a double reaction, "exudative" and "proliferative." The exudative reaction consisted of a pouring out into the pulmonary alveoli of large epithelial-like cells which from their morphology and behavior were unmistakably histiocytes. The proliferative reaction consisted of a multiplication of the cells lining the alveoli, with the formation of microscopic clusters (nodules) composed of these cells. The cells in these areas had undergone some metamorphosis; they were plump, their cytoplasm had acquired here and there a vacuolated appearance.

Some of the alveolar cells in situ had grown larger and had taken up the dye in the regular histiocytic fashion, and certain of the typically "tatooed" as well as the unstained alveolar cells had detached themselves from the alveolar wall to participate in the "alveolar exudate."

It is obvious from these observations that the lungs abound in histiocytes.

2. *"Chronic" Intratracheal Staining of Animals.*—In this final series of experiments the animals were *repeatedly* stained by way of the trachea. Five cubic centimeters of a solution of 1:100 of pyrrol blue was injected daily into the trachea of a rabbit and 2 cc. into the trachea of a guinea-pig on five successive days, and the animals were killed twenty-four hours after the last injection. The last two injections were usually supported less well than the first, the animals showing slight dyspnea, with loss of their usual appetite and liveliness.

Results: Macroscopic Examination.—When the thoracic cavity was opened the lungs did not collapse. They were full and deeply blue, and appeared to be saturated with the dye. The visceral pleura was tense and glistening. The entire organ seemed on palpation to be solidified as in the early stages of lobar pneumonia.

The cut surface of the lung in only a few areas had its normal spongy appearance. On pressure a clear blue frothy fluid could be squeezed out. The mucosa

of the bronchi was unchanged but the lumen contained a colorless thin frothy fluid. There were no signs of inflammation either in the pulmonary parenchyma or in the vessels of the bronchi.

Microscopic Examination.—Sections from different parts of the lungs showed that though the lungs appeared as a solid block of blue tissue, the dye had not penetrated the organs uniformly. As in the previous experiments it was concentrated in definite areas, the difference in the reaction being quantative rather than qualitative. It was, of course, more pronounced around the bronchi and bronchioles

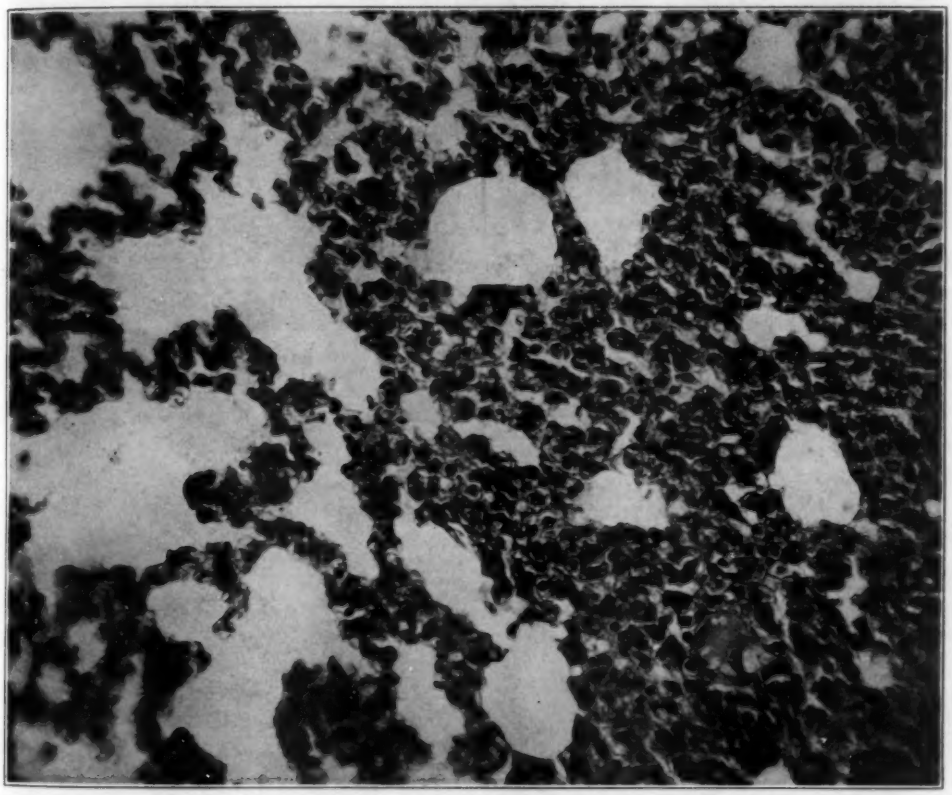

Fig. 2.—Pulmonary tissue from a rabbit repeatedly stained intravitally by way of the trachea with pyrrol blue. A transition zone between distended alveoli having their wall greatly thickened and cellular agglomerations. The alveolar septums merge with the cellular masses which are composed of the cells "lining" the wall of the alveoli. × 300.

and also nearer to the hilus. The microscopic findings can be summarized as follows:

1. The dye had been taken up by the same large cells previously described as having oval or irregularly round nuclei and a relatively large amount of cytoplasm. It was confined to the cellular cytoplasm where it was distributed in the usual histiocytic manner (fig. 1).

2. Swollen alveolar wall cells were seen in almost every microscopic field with a typical histiocytic distribution of the vital dye in their cytoplasm. Not infrequently in areas where the lung had preserved its normal structure these "tatooed" cells were found lying close to the alveolar wall. They appeared to be caught *en flagrant délit* while abandoning their usual seat (fig. 1). In a few instances a tendency to form giant cells of the Langerhans type was noted (fig. 5).

3. As in the previous experiment the reaction was "exudative" and "proliferative." Vitally stained histiocytes could be seen lying free in almost every

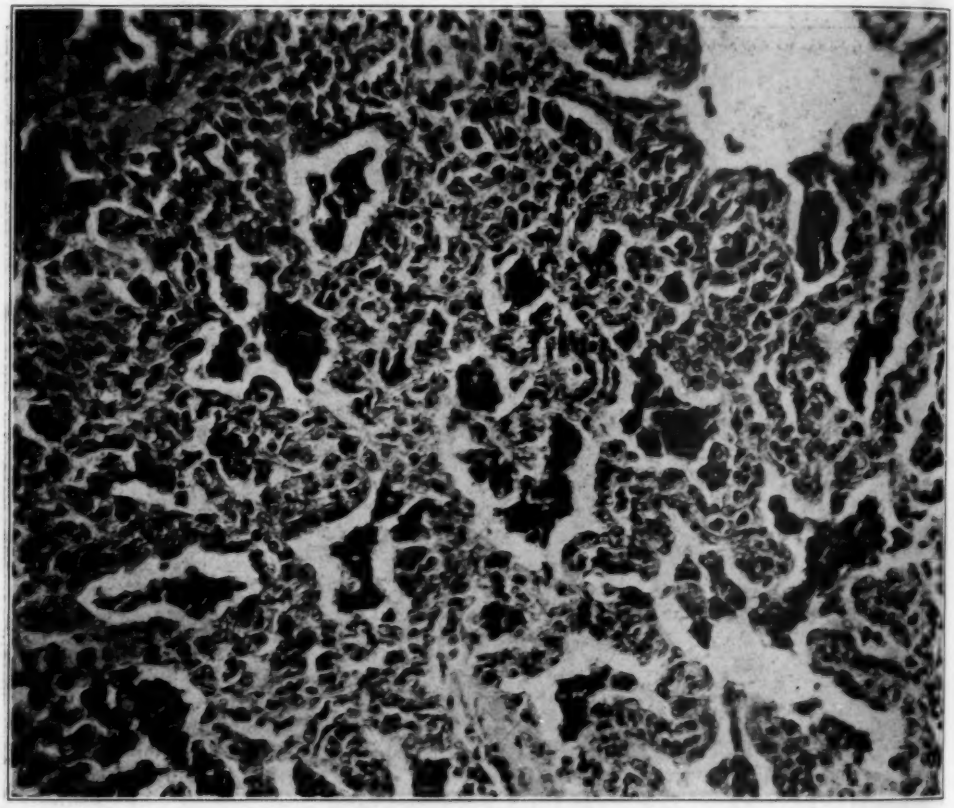

Fig. 3.—Lung tissue from a rabbit repeatedly stained with pyrrol blue by way of the trachea. The normal pulmonary architecture is destroyed. In the remnants of the irregular and disfigured alveoli are seen groups of cells stained in a fashion characteristic of histiocytes. In a few instances clumps of cells loaded with dye have formed agglutinated black masses. × 300.

pulmonary alveolus (figs. 2, 3 and 6). Morphologically they were identical with the "dust cells," the "heart-failure cells," or the large vacuolated cells seen in tuberculous bronchopneumonia.

The cells of the alveolar wall itself had become considerably enlarged and had taken on an aspect resembling the histiocytic cells which were free in the alveoli. Their cytoplasm was frequently vacuolated and they had also apparently increased in number, so that the entire alveolar septum had become many-fold thicker than usual (figs. 1 and 2).

4. Wide areas of the pulmonary parenchyma had altogether lost the normal alveolar architecture. In these areas there was a diffuse cellular agglomeration occupying several low power microscopic fields (figs 2, 3, 4 and 5). When examined with the naked eye these seemingly "consolidated" areas resembled bronchopneumonia patches. But the cells in these areas were not lymphocytes or leukocytes. Moreover, there was no fibrin or serum in the sections, nor could bacteria be identified by Giemsa or Gram stains. The reaction, beyond any question, was not inflammatory in character.

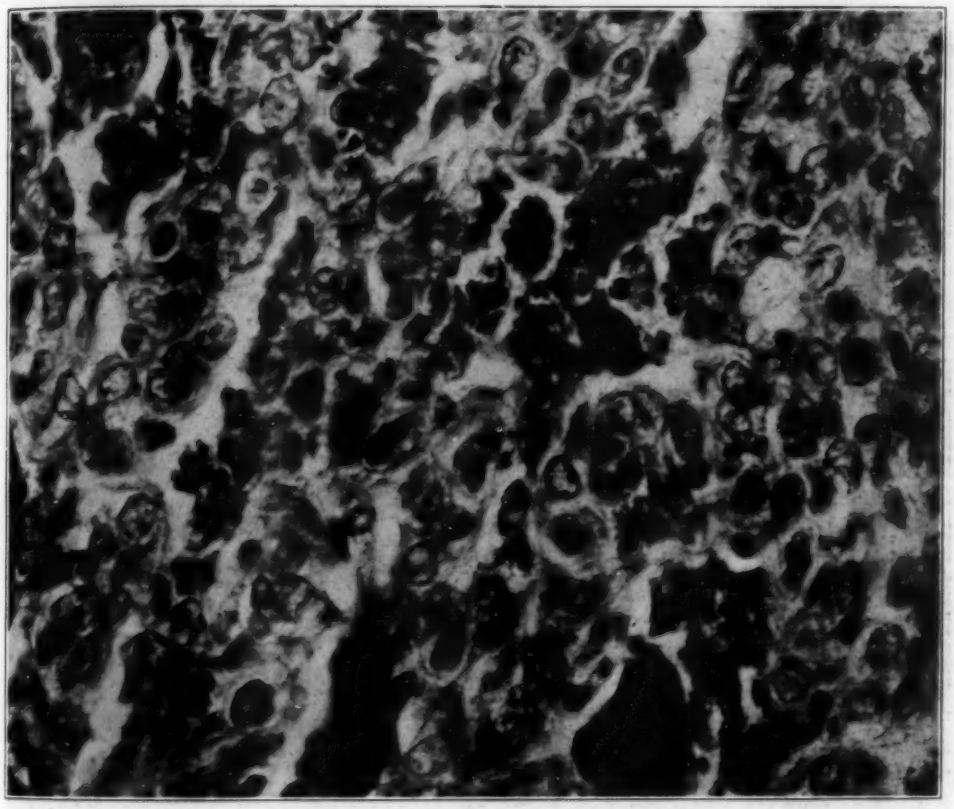

Fig. 4.—Pulmonary tissue from a rabbit treated in the manner indicated. A detail × 850 showing the morphology of the cells—large cells with a foamy cytoplasm and a vesicular nucleus. The vital dye is seen in the cytoplasm as coarse and fine black granules. In areas there are "black patches" composed of apparently dead cells (the nuclei are stained) loaded with stain.

Morphologically, the cells in these areas were epithelial-like with abundant cytoplasm which was frequently vacuolated. Histiocytes which had stored the vital dye in a typical way were found scattered singly and in clusters among these crowds of cells. The typically stained histiocytes and the unstained cells were identical in their finest details (figs. 4 and 5).

On examining the sections at the edge of these cellular masses, one was impressed with the fact that the cells of which they were composed were nothing

other than those "lining" the pulmonary alveoli, which had proliferated under the influence of the dye, forming wide cellular agglomerations (fig. 2).

Comment.—This series of experiments has shown that only the so-called epithelial cells lining the alveolar wall respond to the repeated intratracheal injection of the dye. These cells take up the dye in situ in a specific manner characteristic of the histiocyte; they detach themselves from the septum forming the alveolar "exudate"; they proliferate

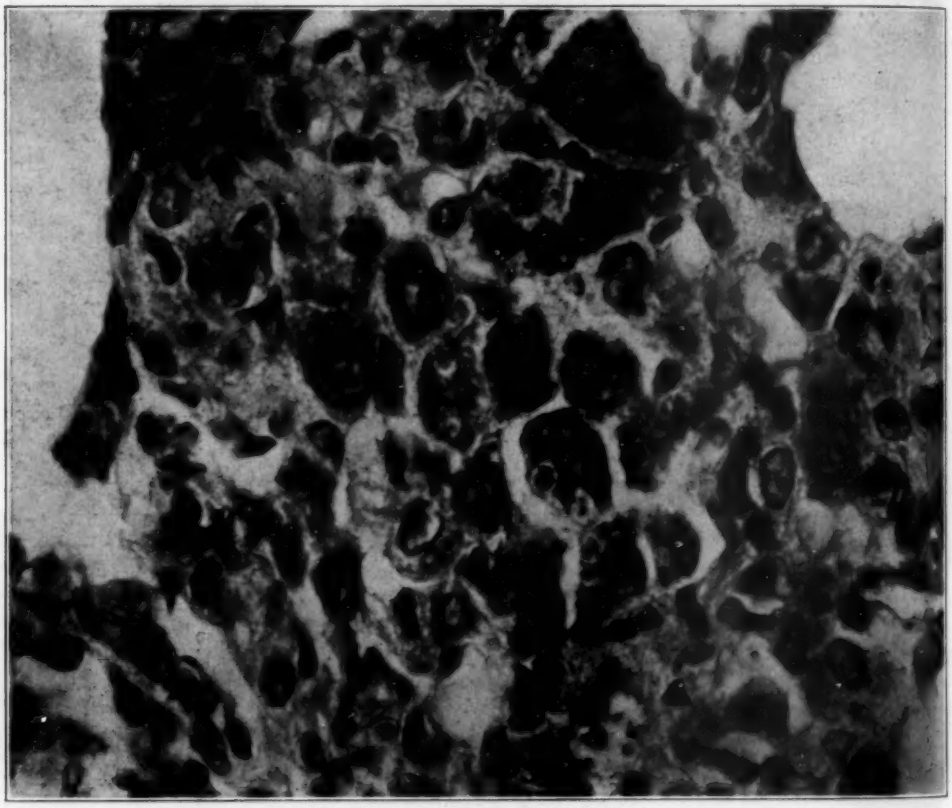

Fig. 5.—Pulmonary tissue from another rabbit treated in the manner indicated. In the upper part of the photomicrograph is seen a large cell with two nuclei which suggests a giant cell. ×850.

with resultant thickening of the alveolar septums and the formation of large "pseudotumorus" masses composed of vitally stained cells and also of unstained cells, with eventual obliteration of the normal pulmonary structure.

DISCUSSION OF EXPERIMENTS

1. *The Nature of the Phagocytic or "Dust Cells."*—The property of phagocytosis and the specific reaction to vital dyes are characteristic of

the cells comprising the so-called reticulo-endothelial system. Morphologic similarities between cells, as already noted, are of only secondary importance. Thus, for instance, the Kupffer cells of the liver and the reticular cells of the spleen differ in shape and in size, yet they are both included in the same system. Apparently, the large cells found in the pulmonary alveoli in some inflammatory and congestive processes belong in the same category, being cells of mesenchymal origin, possessing all the potentialities with which the cells of the reticulo-endothelial system are endowed.

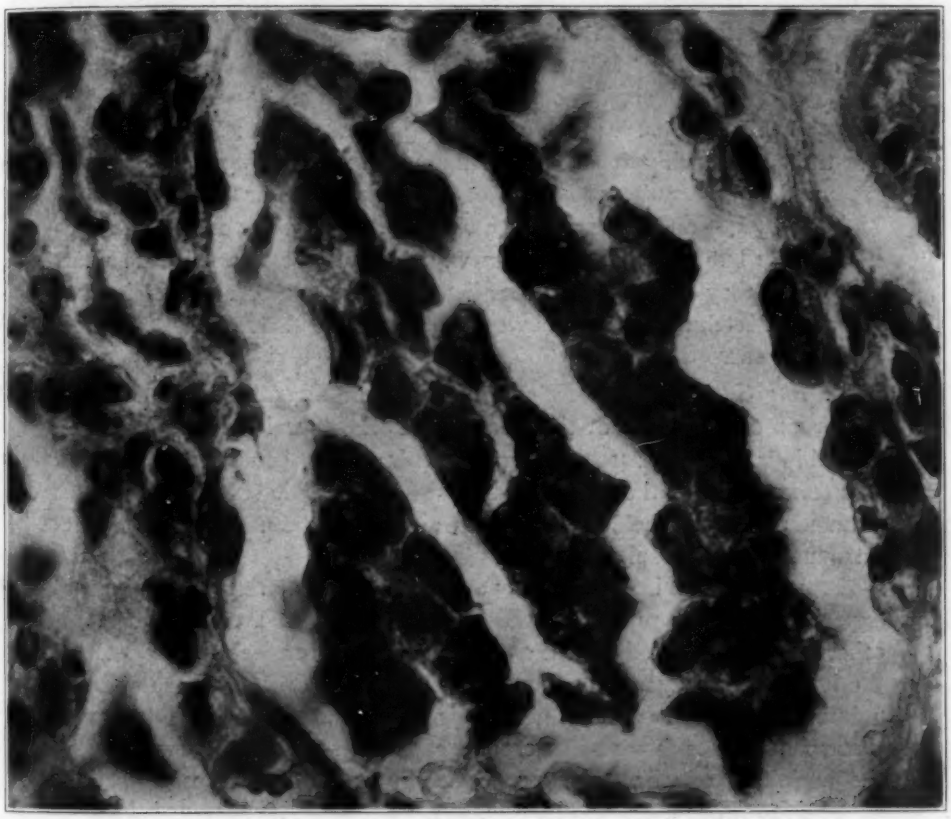

Fig. 6.—A largely distended air sac with cells (macrophages) detached from the alveolar wall and stained in a histiocytic manner. In the right side of the photomicrograph the cells are still attached to the alveolar septum. × 850.

The idea that these cells as they occur in the lungs are essentially phagocytes was first expressed by Metchnikoff who in 1901 made the following statement:[10] "For long the large 'dust cells' of the respira-

10. Metchnikoff, E.: Imunity in Infective Diseases, transl. from the French by F. G. Binnie, Cambridge, at the Cambridge University, 1907.

tory channels were looked upon as being epithelial cells which were capable of taking up carbon particles, micro-organisms and other foreign bodies. In reality these elements are nothing more than white corpuscles [*sic*] that have immigrated into the alveoli and bronchi." He identified these cells with the macrophages and compared them with the Kupffer stellate cells of the liver. In a study of the phenomenon of phagocytosis, Tchistovitch [11] makes practically the same statement, namely, that the destruction of pathogenic microbes which have penetrated into the pulmonary alveoli is effected through the intermediary of the macrophage. "This cell" he states, "frequently contains pigment and is identical with the 'dust cell.'" A similar opinion has also been expressed by Aschoff who quotes [12] the observations of certain Japanese workers whose methods though differing from those employed in the experiments herein presented, led the authors to arrive at conclusions similar to my own.

Figures 1, 4 and 5 demonstrate clearly, not only by the morphology of the cells but also by the way in which they have taken up the vital stain, that they are, beyond question, wandering macrophages in the sense of Metchnikoff (histiocytes of Aschoff and Kiyono) and not epithelial cells.

2. *The Genesis of the Phagocytic or "Dust Cells."*—For a detailed discussion of the origin of the macrophages in general the recent papers by Sabin [13] and her associates, and by Maximow [14] may be consulted. The conceptions of the source of the large phagocytic cells found in the pulmonary alveoli held by earlier writers has been outlined in the introductory paragraphs.

It seems most improbable that the pulmonary macrophage in the experiments herein reported could be brought by the blood stream from other parts of the body, such as the spleen or liver, being attracted to the lungs by the dye. The examination of other organs of the stained animals fails to reveal any histiocytic activity outside the lungs, and that such an abundance of macrophages could reach these organs from the periphery one or two hours following the intratracheal injection of the dye seems most unlikely. So far as the spleen is concerned, Foot [15]

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11. Tchistovitch, N.: De phénomènes de phagocytose dans les poumons, Ann. de l'Inst. Pasteur **3**:337, 1889.

12. Aschoff (footnotes 4 and 6).

13. Sabin, Florence R.; Doan, C. A., and Cunningham, R. C.: Discrimination of Two Types of Phagocytic Cells in the Connective Tissues by the Supravital Technique, Contrib. Embryol. Carnegie Inst., Washington **16**:125, 1925.

14. Maximow, A. A.: Tuberculosis of Mammalian Tissue in Vitro, J. Infect. Dis. **34**:549, 1924.

15. Foot, N. C.: Changes in the Distribution of Colloidal Carbon Noted in the Lung of Rabbits Following Splenectomy, J. Exper. Med. **37**:139, 1923.

and Wislocki [16] have shown that removal of this organ is not followed by any decrease in the number of macrophages found in the lungs under the conditions of these experiments. In his observations on the origin of the macrophages in the lungs of frogs Lewis [17] concluded that the liver and spleen do not play any rôle in providing the lungs with these cells. Even more conclusive are the observations of Lang,[18] who made cultures of lung tissue infected with tubercle bacilli and arrived at conclusions from his observations in vitro, which are in accord with mine as drawn from the experiments in vivo, namely, that the macrophages are of local origin. Under the conditions of his experiments it was impossible that the phagocytic cells could have been supplied by any outside source. It is believed, therefore, that the histiocytes present in the pulmonary alveoli following repeated intratracheal injections of pyrrol blue are not "imported" but are locally produced. There are three possible sources of these cells: (*a*) the bronchial epithelium; (*b*) the endothelium lining the capillary vessels, and finally (*c*) the cells lining the wall of the alveoli.

(*a*) A superficial examination of the bronchial epithelium is sufficient to persuade one that this structure remains entirely indifferent to the introduction of the dye into the lungs (fig. 7). Opinion in this respect is unanimous.

(*b*) The possible rôle of the endothelium lining the capillaries in the formation of the histiocytes has been emphatically opposed by Maximow,[14] and by Westhues [6] from Aschoff's laboratory. The experiments herein reported seem to corroborate fully the opinion of these workers. In none of the numerous sections of tissue studied has there been any suggestion that the vascular endothelium is involved in the reaction.

(*c*) The opinion that the pulmonary alveoli are lined with a single layer of epithelial cells has become firmly fixed in the minds of most persons. Consequently, the view that the pulmonary macrophages could possibly originate from these cells has been incomprehensible. However, the notion that the pulmonary alveoli are so lined with a single layer of respiratory epithelial cells is probably based on a misconception. Histologic investigations of the lungs by the use of silver nitrate methods have shown that there are two elements lining the alveolar spaces, small

16. Wislocki, G. B.: On the Fate of Carbon Particles Injected into the Circulation with Especial Reference to the Lungs, Am. J. Anat. **32**:423, 1924.

17. Lewis, M. R.: Origin of Phagocytic Cells in Frogs' Lungs, Bull. Johns Hopkins Hosp. **36**:361, 1925.

18. Lang, F. J.: Ueber Gewebskulturen der Lunge, Arch. f. exper. Zellforschung **2**:93, 1925.

irregularly round or polygonal nucleated cells, and large irregular plate-like cells without nuclei, which vary greatly in size—from 40 to 100 microns. The nucleated cells, according to Stewart [19] and Ogawa,[20] do not line the alveolar space as an uninterrupted syncytium, but are found singly or in groups of from two to five. Often they lie in the sinuosities of the extremely tortuous capillaries of the alveolar septums, giving the impression of being actually within the wall of the alveolus.

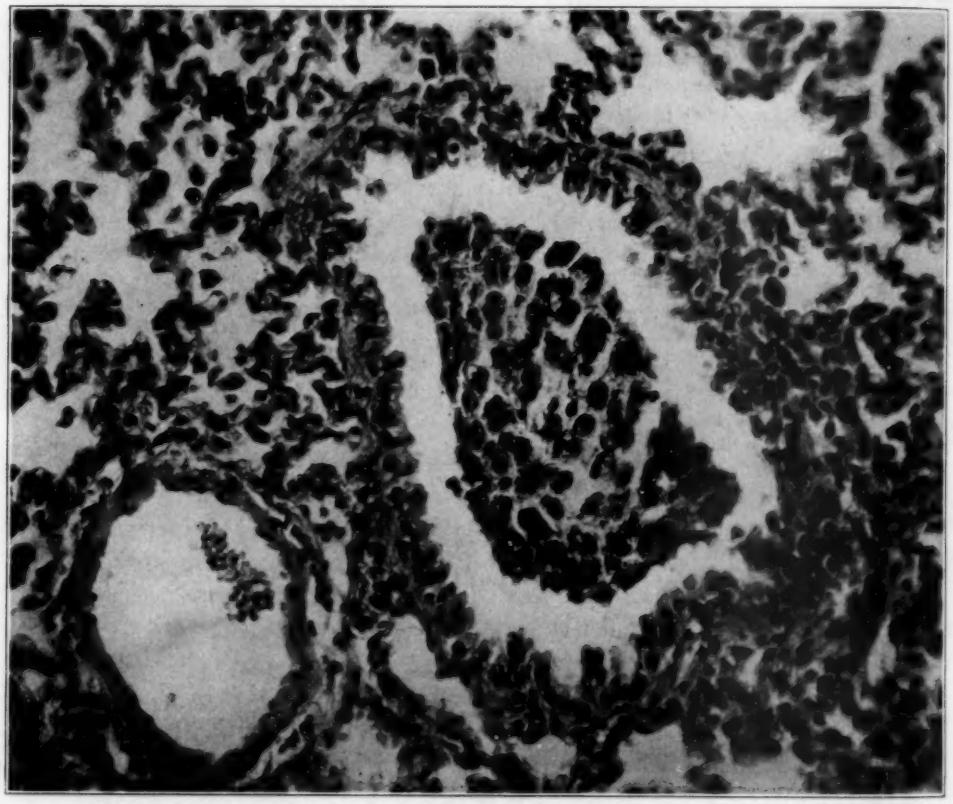

Fig. 7.—A bronchus from a rabbit repeatedly stained with pyrrol blue by way of the trachea. The bronchial epithelium is intact. The bronchial lumen contains a group of histiocytes which have stored the dye in a characteristic manner. The pulmonary alveoli around the bronchus contain vitally stained "desquamated" nucleated alveolar cells. × 300.

The genesis of the pulmonary macrophages from the nucleated alveolar cells is probable in that there seem to be no other elements in the lung whence they could arise, and in the experiments quoted it was

19. Stewart, F. W.: A Histogenetic Study of the Respiratory Epithelium, Anat. Record **25**:181, 1923.

20. Ogawa, C.: Contribution to the Histology of the Respiratory Spaces of the Vertebrate Lungs, Am. J. Anat. **27**:333, 1920.

obvious that the reaction to the vital dye is participated in by these cells alone. Ordinarily small, varying in size from 5 to 15 microns, they become enlarged and take on the aspect of epithelial-like cells which detach themselves from the alveolar wall and lie free in the alveoli. The same alveolar cells storing the dye in a characteristic manner are seen quite often to lie close to the alveolar septum or to be partly detached from it.

Reactions similar to those described have been noted by others, as by Briscoe [2] in his experiments with intratracheal injections of bacteria or pigeons' red corpuscles. In recent experiments with vital staining in tuberculosis, Jaffé [21] noticed in the liver a reaction of the Kupffer cells similar to that of the alveolar cells seen in my experiments.

From the foregoing it is safe to say that the large phagocytic cells ("dust cells") found in the pulmonary alveoli take their origin from the nucleated cells lining the alveoli.

3. *The Nature of the Nucleated Alveolar Cells.*—Experiments herein reported indicate that the nucleated cells of the alveolar wall are the source of the ameboid macrophages (histiocytes) found in the pulmonary alveoli.

What, then, is the nature of the nucleated alveolar cells themselves? *A priori* it should be assumed that the mother cells belong to the same cellular strain and that the nucleated cells of the alveolar wall are also histiocytes. Moreover, their morphology, their phagocytic avidity and their vital staining peculiarities definitely indicate that they belong to the reticulo-endothelial system, in other words that they are of mesenchymal origin.

That these cells are essentially phagocytic is unanimously agreed. Büchner [22] was one of the first to note that when spores of the anthrax bacillus were inhaled into the rabbit's trachea the spores were "phagocytosed" almost exclusively by the "epithelial" [sic] cells of the wall of the pulmonary alveoli. Fleck [23] observed the same reaction in instances of intratracheal infection with *Staphylococcus pyogenes,* and Laehr [24] with *Staphylococcus aureus.* Briscoe,[2] in his experiments with the intratracheal injection of *Bacillus mesentericus vulgaris,* affirms that the alveolar cells are energetic in ingesting the bacilli.

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21. Jaffé, R.: Studies on the Vital Staining in Experimental Tuberculosis, Am. Rev. Tuberc. **13**:97, 1926.

22. Büchner, H.: Untersuchungen über den Durchtritt von Infectionserregern durch die intakte Lungenoberfläche, Arch. f. Hyg. **8**:147, 1888.

23. Fleck: Die Acute Enzündungen der Lunge, Dissertation, Bonn, 1886.

24. Laehr, G.: Ueber den untergang des Staphylococcus pyogenes aureus in den durch ihn herforgerufenen Enzündungsprocessen der Lunge, Dissertation, Bonn, 1887.

Timofejewski and Benevolenskaja [25] have recently investigated in vitro the reaction of the lung tissue to infection with living tubercle bacilli. The striking feature in the cultures was the particular activity of the "epithelial" cells lining the pulmonary alveoli. A few hours after the inoculation these cells and no other begin to swell and to separate themselves from the wall, invading the alveoli; they produce pseudopodia showing active motion and avid phagocytosis of red cells and leukocytes.

A similar phagocytic avidity, as far as it is known today, is proper to the histiocytic type of cells only. In addition to phagocytosis in the experiments herein reported, the unusual proliferation of the cells lining the alveoli within from two to three days following the first injection of the dye is incompatible with the known characteristic of an epithelial cell, whereas cells of mesenchymal origin do possess such properties, as shown by intravenous injections of vital stains and bacteria (Goldmann,[3] Kuczinski,[26] Oeller [27]). Again, the fashion in which they have stored the vital stain was conclusive evidence that they are histiocytic. As already noted in areas where the dye was concentrated, and also in places where the vital stain could not be seen microscopically, the alveolar cells in situ have taken up the blue stain, storing it characteristically in their cytoplasms as fine droplets of various size.

Finally, morphologic similarities between the histiocyte and the "alveolar wall" cell after they have been activated by the dye, though believed to be of minor importance, are none the less impressive and cannot be entirely disregarded as a criterion, when coupled with the physiologic resemblances.

The interpretation of the results obtained is obviously open to objection on embryologic grounds. Embryology teaches that the air sacs of the embryo are lined with a single layer of cuboidal epithelial cells. It is assumed that as a result of the first respiratory effort certain of these cells become flattened and some lose altogether their nuclei, thus leading to the formation of the *anucleated platelike cells* of the functioning alveolus. The abrupt flattening of the cuboidal cells following the first respiratory movement and the formation of anucleated cells has, however, never been plausibly explained. The fact that the cuboidal cells in the embryonic air sac lie directly on the septum without having a basal membrane makes their epithelial nature doubtful. Again,

25. Timofejewski, A., and Benevolenskaja, S. W.: Zur Frage über die Reaction von Gewebskulturen auf Tuberkuloseinfection, Virchows Arch. f. path. Anat. **225**:613, 1925.

26. Kuczinski, M.: Edwin Goldmann's untersuchungen über Zelluläre Vorgänge, etc., Virchows Arch. f. path. Anat. **239**:285, 1924.

27. Oeller, H.: Experimentelle Studien zue Pathologischen Physiologie des Mesenchyms und seiner Stoffwechselleistungen bei Infectionen, Krankheitsforschung **1**:28, 1925.

the lack of a transitional epithelium between the bronchiolic pavement epithelium and that of the supposed cuboidal alveolar epithelium speaks against the continuity of the same strain of cells. Finally, it has been accepted that in birds, in the bat and in the mole the respiratory epithelial lining of the air sac is wanting.

The presence of an intermediary epithelial layer between the alveolar air and the mesenchyme is consequently not a *conditio sine qua non* as it was thought to be by former writers.

CONCLUSIONS

1. The phagocytes or "dust cells" in the pulmonary alveoli in inflammatory and congestive processes are macrophages or histiocytes, and therefore cells of mesenchymal origin.

2. These cells originate from the nucleated cells, commonly spoken of as the (respiratory) epithelial cells lining the wall of the pulmonary alveoli.

3. The so-called epithelial cells lining the pulmonary alveoli are to all appearances not epithelial but cells of mesenchymal origin—that is to say they are histiocytes, and belong to the reticulo-endothelial system.

THE MICROSCOPIC ANATOMY OF INFANTILE AMAUROTIC IDIOCY

WITH SPECIAL REFERENCE TO THE EARLY CELL CHANGES AND THE INTRACELLULAR LIPOIDS *

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It is generally agreed that amaurotic idiocy is primarily a developmental disorder with secondary degenerative changes which involve the ganglion cells diffusely. The fundamental microscopic anatomy is, however, a matter of discussion, principally because material is usually studied in the late stages or when secondary cellular disintegration has become widespread.

Fortunately, the two cases reported here have revealed early changes, so that the development of the characteristic pathologic condition could be studied in its successive stages.

REPORT OF CASES

CASE 1.—A female child, aged 13 months, born normally, never had been able to sit up or to make any attempt at talking. The child was breast fed for one year, and had her first tooth at 10½ months. At the age of 2 months it was noticed that she did not laugh or smile or follow a bright light with her eyes. She never could reach for objects or hold things in the hands.

The infant was well nourished. The anterior fontanel was open. A deep red and prominent macula lutea was the only physical abnormality. She did not pay any attention to external stimuli. Nine months later, on readmission, the child could not swallow food, but retained it in the mouth. For two weeks there had been insomnia and constipation. The child soon became comatose, with staring eyes and absent reflexes, the extremities became rigid, and twitchings of the facial muscles were noted. Death occurred from pulmonary edema at the age of 22 months.

Necropsy revealed a congenitally thin membranous interventricular septum of the heart. Incomplete lobation of the lungs with hemorrhagic infarcts and edema, a small fibroma of the medulla of the left kidney and status thymicolymphaticus were also noted.

CASE 2.—A female child, aged 17 months, with a normal birth history, had been able to sit up and was bright and cognitive of her environment at 4 months. At 7 months she could no longer sit up, became mentally dull, failing to recognize objects, and was very irritable. The lower extremities were spastic, with exaggerated reflexes. The maculae luteae were white and contained cherry red centers; the optic disks were atrophic. Death occurred from bronchopneumonia.

Both brains will be described together, since they are similar in most respects.

* From the Syndacker Fund and Neurological Service of the Michael Reese Hospital, the Sarah Morris Hospital for Children and the Nelson Morris Institute for Medical Research.

NECROPSY OBSERVATIONS

Macroscopic Examination.—The brains were of normal size but distinctly hard. The cerebral convolutions were well marked and the sulci deep. The convolutions revealed many gross abnormalities in position and size, and they were asymmetrical in both brains. In case 2 the convolutions of one hemisphere were broad and flat and much larger than those of the other hemisphere. The brains retained their shape, as though hardened in formalin for weeks, and cut with greatly increased resistance. The only gross alteration noted on the cut surfaces was the similarity of color of the gray and white matter. The optic chiasm and nerves appeared thinned. In case 1 the cord had a fetal lateral sulcus and the cerebellum revealed, on stripping its pia, abnormally wide sulci and thin foliae.

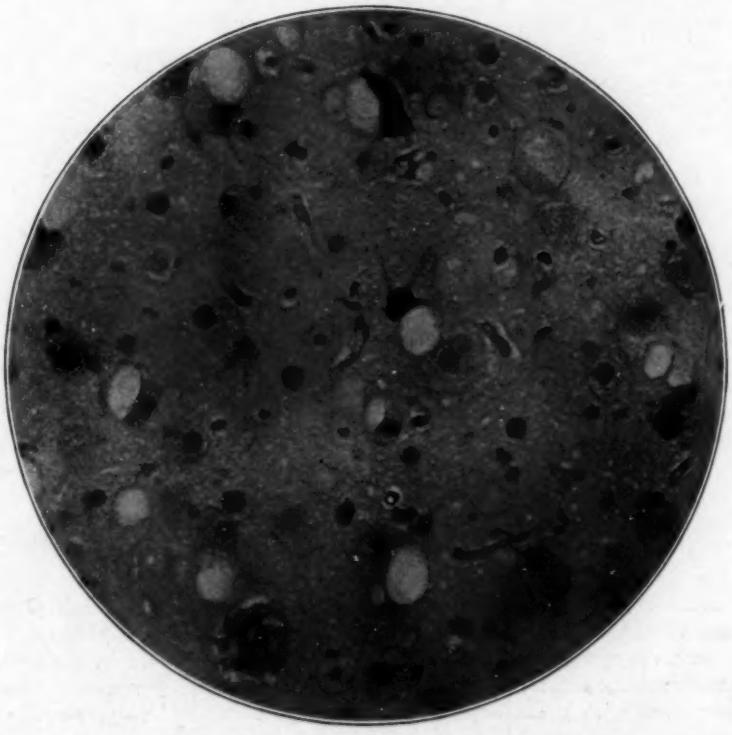

Fig. 1 (case 2).—Temporal cortex; several ganglion cells of normal size and shape, and many swollen cells with granular cytoplasms are present; the large pale areas are gitter cells. Cresyl violet stain. × 300.

Microscopic Examination.—Ganglion cells: Repeated attempts failed to bring out details with toluidin blue. With cresyl violet, however, most of the ganglion cells were seen to be pear-shaped, with the nucleus displaced toward the apical dendrite, and the cytoplasm filled with golden green material. In only certain scattered cortical areas was the architectonic structure somewhat preserved, because of the presence of cells apparently normal on low power examination (fig. 1). These, however, revealed a gradual transition toward the final swollen cell. They have been studied in detail with Bielschowsky and cresyl violet stains and for convenience of description are divided into four groups.

1. Some of the cells were of normal size, angular in form, had processes which were visible for a long distance, and contained sharply defined Nissl bodies (fig. 2). In the cytoplasm also were well formed, deeply hyperchromatic Nissl bodies. Between them in the "ungefärbten Bahnen" the cytoplasm assumed a homogeneous pale blue stain. Bielschowsky preparations, however, revealed normal neurofibrils passing through the cells in a normal manner. The nucleus was markedly swollen, filling most of the cell, and its membrane was sharply defined and regular. The nucleolus was large and intensely blue, while the karyoplasm stained a lighter blue and contained heavy chromatin masses within it about the nucleolus.

2. Cells of the foregoing description apparently became altered gradually (figs. 3 and 4). At the base of the cell in the region of the axonal hillock a golden green substance shone between the hyperchromatic Nissl bodies. At first this

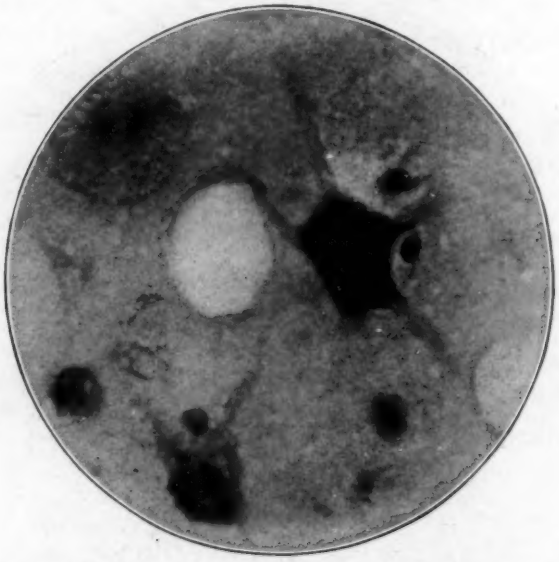

Fig. 2.—A cortical ganglion cell of normal size and shape with processes sharply visible, from the same field as figure 1. The Nissl bodies are hyperchromatic, the cytoplasm, homogeneous blue; the nucleus is swollen and hyperchromatic; to the left a large gitter cell and at the periphery a greatly distended ganglion cell with granular cytoplasm. Cresyl violet stain. × 800.

was limited to the normal inter-Nissl substance, but later the Nissl bodies became replaced by the golden lipoid, which gradually extended to fill the entire cell. When the base of the cell alone was affected the lipoid was enmeshed in coarse thick strands, forming vacuoles which were seen clearly in Bielschowsky preparations (fig. 5).

3. Increasing in amount, the pigment filled the entire cell, pushing the nucleus toward the apical dendrite. The cells became swollen to two or three times the normal size. The Nissl substance disappeared and was replaced by a finely reticulated network, with uniformly appearing nodal points, in contrast with the earlier coarse vacuoles (fig. 6). This net was also argentophilic. The entering large neurofibrils were decreased in number and those present were pushed to the

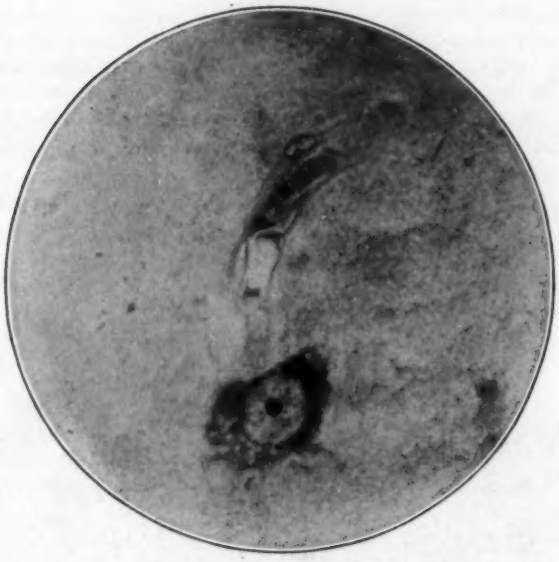

Fig. 3 (case 2).—Lipoid enclosed in a coarse mesh at the base of a ganglion cell from the parietal lobe; the remainder of the cell contains normal Nissl substance. Cresyl violet stain. × 800.

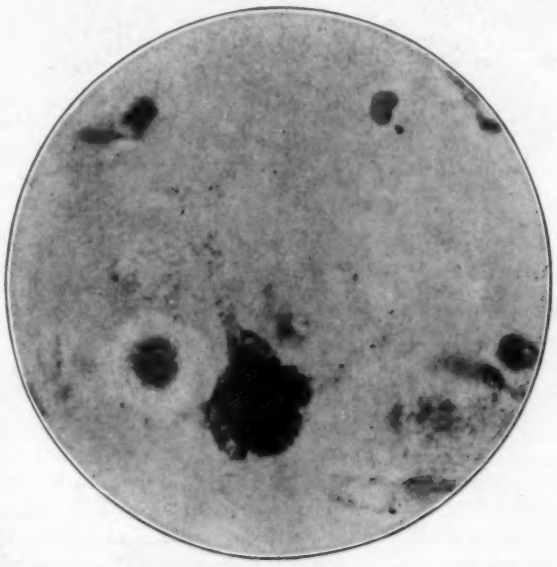

Fig. 4.—Ganglion cell with a large hyperchromatic nucleus; a small amount of lipoid is present at the base of the cell between the Nissl bodies. Cresyl violet stain. × 800.

periphery of the cell by the lipoid material. In many cells there was a perinuclear mass of dark chromatin which faded indefinitely into the reticular cytoplasm, an appearance described also by Poynton, Parsons and Holmes[1] (fig. 7). Definite Nissl structure was not seen in this mass. Such cells contained a relatively lighter staining nucleus, which had an irregular or often indistinguishable membrane. The nuclear chromatin frequently was apparently continuous with the perinuclear chromatin. Cells not having any perinuclear mass had a sharply defined nuclear membrane (fig. 6).

4. The terminal stage gave the characteristic sievelike structure to the cortex (figs. 1 and 2). The cells were huge, usually well rounded, and had a thick

Fig. 5.—The central cell is of normal size; its upper portion contains normal neurofibrils, but at the base there is an early accumulation of lipoid; the cell at the right reveals the incoming neurofibrils, in this late stage, pushed to the periphery; the large cells to the left show the granular remnant of the cytoplasmic reticulum only at the cell periphery. Bielschowsky stain. × 415.

membrane. The nucleus was at one pole and, in proportion to the cell size, was relatively smaller than before. The cytoplasm was filled with fine dustlike basophilic and argentophilic granules, without definite form, embedded in a background of golden pigment. No network remained, and only a few neurofibrils

1. Poynton, F.; Parsons, J., and Holmes, G.: A Contribution to the Study of Amaurotic Family Idiocy, Brain **29**:180, 1906.

were seen pressed against the cell periphery. The granules in many cells were present only about the cell membrane and nucleus, apparently having disappeared from the central portion (fig. 5). A few cells in the cortex, but many in the thalamus were disintegrating, undergoing neuronophagia by many surrounding glia cells.

Neuroglia: The glia studied in Alzheimer-Mann and Victoria blue preparations revealed changes of a secondary nature (figs. 1, 2 and 4).

About the ganglion cells were usually several large glia cells of the cytoplasmic type, whose nuclei were large and progressively altered. Their cytoplasm contained a lipoid material, similar to that within the ganglion cells, within a fine reticulum. Few free rounded "gitter," or compound granular, cells were seen; these were present, however, about disintegrating ganglion cells and about the vessels in the deeper myelin layers. The glia cells exhibited a tendency to be

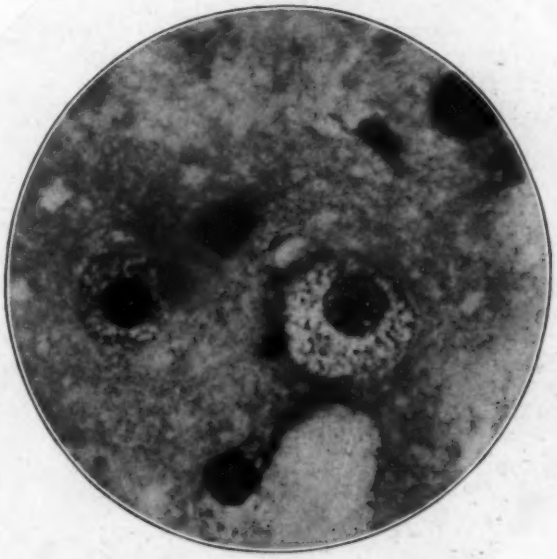

Fig. 6.—Ganglion cells with a finely meshed cytoplasmic reticulum containing lipoid material; the hyperchromatic nuclei have sharply defined membranes. Cresyl violet stain. × 800.

arranged in groups, the so-called "Glia-Rasen" of Nissl. They were of the cytoplasmic type, and either maintained their own individuality or had a common cellular membrane. The subcortical glia layer was not increased, but the subependymal region, especially in the thalamic areas, was thickened by fibrous glia. Monstral glia cells were not seen.

Nerve fibers: The axones were well preserved (fig. 5). Aside from occasional slight swelling and tortuosity of the fibers, they did not exhibit any degeneration. The neurofibrils appeared normal within the axones, and in the earlier stages passed through the cells in a normal manner. Later they were pressed to the cell periphery, but did not seem to take any part in the formation of the intracellular net. The dendrites had numerous and large swellings. These had the same granular appearance as the swollen ganglion cells, and within the knob-like swellings the neurofibrils were pressed to the periphery.

Myelin sheaths: Visible degeneration of the myelin sheaths was not observed, but there was a marked thinning in the radiating cortical fibers. Scarcely any myelinized tangential fibers were seen. Most of the long descending tracts appeared poor in myelinized fibers and the thalamic and hypothalamic regions revealed a marked deficiency in medullary sheaths.

Mesodermal structures: In the pia arachnoid there were areas of thickening which contained much fibrous tissue. Within these areas there were large histiocytes and a few round cells. Perdrau and van Gieson stains did not reveal any excess of vascular connective tissue. About the blood vessels of the deep myelin layers in the intra-adventitial spaces there were many compound granular cells.

Fig. 7 (case 1).—Cerebellum; the Purkinje cells are swollen and pear-shaped; the cytoplasm is dustlike, the nucleus does not have a sharp membrane but blends with the perinuclear mass; the granule layer is markedly narrowed and the cells are widely spread, but glial proliferation is absent. Bielschowsky stain. × 140.

Cerebellum: In case 1, in which gross thinning of the foliae was observed, the granular layer was about half the normal thickness (fig. 7). The granule cells were more widely spaced but of normal size and contour, and glial proliferation was not present. In both cases the Purkinje cells were large and bottle-shaped; their dendrites, including all the branches, were swollen from the neck of the cell to the cerebellar surface, so that they resembled large branching antlers (fig. 8). In place of intradendritic neurofibrils there was a fine dustlike material.

The nuclei were pyknotic and blended into a perinuclear dark mass which stained darkly with the cresyl violet and Bielschowsky methods.

Retinae: The retinae were removed early enough to prevent postmortem changes. Section through the macula of only one retina was possible.

In case 1 the optic nerve head was a pinhead sized, elevated disk, with a brown depression. The macula was elevated and had a yellow tint; in the center was a pinpoint depression. Microscopically the optic nerve was thinned and contained an increase of fibrous tissue at its head. The superficial nerve fibers of the retina were almost completely replaced by glial tissue (fig. 9). Almost all of the

Fig. 8 (case 2).—Cerebellum; the wide granule layer should be contrasted with that in case 1; the dendrites of the Purkinje cells are uniformly swollen. Bielschowsky stain. × 140.

ganglion cells were absent. Those present were swollen and resembled the cortical cells. The cytoplasm stained a homogeneous pale blue with Nile blue. The other retinal layers were normal.

In a section through the macula in case 2, the fibrils in the ganglion cell layer were absent and were replaced by glia. Normal ganglion cells were not present, but a few widely separated, sharply outlined large cells contained a finely meshed cytoplasm and an eccentric nucleus. The peripheral and macular regions were equally affected. The other retinal layers were normal and the pigment layer was not proliferated.

Lipoids: The following methods, with the differential results which they are supposed to give, were used in the study of the lipoids.

Nile blue stains fatty acids blue, neutral fat pink and mixtures purple (Lorraine Smith[2]).

Fatty acids stain with hematoxylin after mordanting with copper acetate (Klotz[3]).

Fatty acids, cerebrosides and lipochrome pigment remain insoluble in alcohol after twenty-four hours in saturated zinc acetate. Cerebrosides are then soluble in equal parts of methyl alcohol and chloroform, and the fatty acid in equal parts of acid alcohol and ether. Lipochrome remains insoluble (Hurst[4] after Ciaccio).

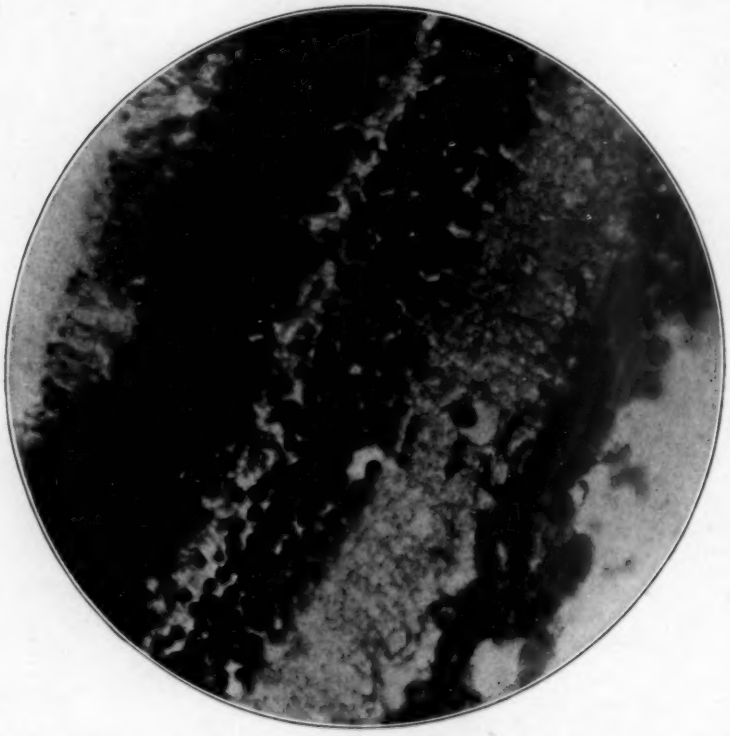

Fig. 9 (case 1).—Retina; marked degeneration of the ganglion cell layer with glial replacement; a single displaced ganglion cell is swollen with lipoid material; all the other layers including the rods and cones are normal. Cresyl violet stain. × 375.

Increasing oxydation of lipoids by increasing time of bichromate mordanting and subsequent hematoxylin staining by the Weigert method gives the following differentiation: Triolein and oleic acid mixtures stain from the fifth to twenty-

2. Smith, J. L.: On the Simultaneous Staining of Neutral Fat and Fatty Acid by Oxydizing Dyes, J. Path. & Bact. **12**:1, 1908.

3. Klotz, O.: Studies Upon Calcareous Degeneration, J. Exper. Med. **8**:322, 1906.

4. Hurst, E. W.: A Study of the Lipoids in Neuronic Degeneration and in Amaurotic Family Idiocy, Brain **48**:1, 1925.

fourth day of mordanting, triolein and cholesterol mixtures from the third to twenty-fourth day, oleic acid and cholesterol mixtures from the first to tenth day, and pure cholesterol not at all (Smith and Mair[5]).

Hurst[4] (after Cramer) records lipoid reactions and solubilities as shown in the table.

In the cases studied, scharlach R-hematoxylin stained most of the mass that filled the entire ganglion cell cytoplasm a faint orange red. Few anisotropic globules were present Most of the glia cells stained in the same manner, but many satellites and rounded gitter cells about the deeper vessels, especially in the cerebellum, contained bright red, coarse globules. The "Glia Rasen" contained a pale orange red substance.

Acetone removed the bright red portion of the globules in the glia. The ganglion cells stained more faintly and the granules were no longer doubly refractile. The granules were not so closely packed.

Alcohol removed some but not all of the red from the glia. The granules within the ganglion cells remained unchanged.

Chloroform removed all but a faint residue in the cells, but left the glia filled with a yellow material. Hot xylol left a finely granular residue stained pale yellow in the cells, whereas the glia still contained coarse, faint yellow globules.

Lipoid Reactions and Solubilities (Hurst)

	Scarlet	Doubly Refractile	Osmic Acid	Osmic after Chrome	Acetone	Alcohol	Chloroform
True fats	+	—	+	+	+	+	+
Cholesterol	—	+	+	—	+	+	+
Cholesterol esters	+	+	+	—	—	—	+
Phosphatids	—	+	+	—	—	+	+
Cerebrosides	—	+	+	—	—	—	+
Cholesterol and fatty acid mixtures	—	+	+	+	—	+	+

After mordanting with zinc acetate, treating with alcohol removed the red tinge from the gitter cells, but the yellow granules of glia and ganglion cell were unaffected. Treating with equal parts of methyl alcohol and chloroform or with acid alcohol and ether removed most of the scharlach R stainable substance, but there constantly remained a small amount of faint yellow material.

Nothing stained with osmic acid after chromification. Without the initial chrome treatment the cells and glia became a homogeneous gray black.

Nile blue stained the ganglion cells a diffuse pale blue, while the perineural and perivascular gitter cells stained a deep blue and revealed coarse globules.

Successive mordanting with bichromate, and subsequent staining by Weigert's method, revealed a faint stain, which began in the large cortical and Purkinje cells on the third day of mordanting. This obtained its maximum intensity on the fifth day, with fading beginning on the ninth day. The small striatal

5. Smith, J. L., and Mair, W.: An Investigation of the Principles Underlying Weigert's Method of Staining Medullated Nerves with a Note on the Staining of Fats by Potassium Dichromate and Hematoxylin, J. Path. & Bact. **13**:14, 1909.

cells were faint on the fourth day and well stained on the fifth day. Fading of the myelin sheaths began on the tenth day. The glia contained large coarse granules reacting similarly to the large ganglion cells. Fading did not take place uniformly, a few stained globules were visible in the cells several days after the main contents had disappeared. On the day of maximal staining the cells contained large blue globules, which filled the entire cell uniformly up to the nuclear membrane.

COMMENT

The pathologic observations in these two cases were typical of amaurotic family idiocy. The status spongiosus, as described by Bielschowsky [6] and Globus,[7] was not noted, nor were there seen the monstral glia cells found by Schaffer.[8] The decrease of the granular layer of the cerebellum was not similar to the severe cerebellar condition in Bielschowsky's and Greenfield and Holmes' [9] cases, since the glia was not proliferated. The process resembled a developmental defect more than an active process.

In the thalamus, normal cells were not seen, many were completely disintegrated, and neuroglial proliferation was present. Schaffer [8] originally described marked loss of myelin substance in the thalamus, and Hassin [10] recently localized the most severe changes in his case in that region. The loss of so many cerebral connections of the optic thalamus may mean that in this ganglion there is added to the primary pathologic condition, a secondary degeneration of the "Grosshirn Anteile."

Early in his studies, Schaffer utilized amaurotic idiocy for the study of the endocellular and pericellular nets, since he believed that the cell swelling made them more visible. He, Sachs and Strauss [11] and Vogt [12] considered the intracellular net to be the neurofibrillar net described by Bethe [13] as the intracellular conducting apparatus continuous with the peripheral neurofibrils. They compared the perinuclear dark ring to

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6. Bielschowsky, M.: Ueber spätinfantile familiäre amaurotische Idiotie mit Kleinhirnsymtomen, Ztschr. f. d. ges. Neurol. u. Psychiat. **50**:7, 1914.

7. Globus, J.: Ein Beitrag zur Histopathologie der amaurotischen Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **85**:424, 1925.

8. Schaffer, K.: Zur Pathogenese der Tay-Sachschen amaurotischen Idiotie, Neurol. Centralbl. **24**:836, 1905.

9. Greenfield, J., and Holmes, G.: The Histology of Juvenile Amaurotic Idiocy, Brain **48**:183, 1925.

10. Hassin, G.: A Study of the Histopathology of Amaurotic Family Idiocy (Infantile Type of Tay-Sachs), Arch. Neurol. & Psychiat. **12**:640 (Dec.) 1924.

11. Sachs, B., and Strauss, I.: The Cell Changes in Amaurotic Idiocy, Brain **48**:183, 1925.

12. Vogt, H.: Familiäre amaurotische Idiotie, histologische und histopathologische Studien, Arch. f. Kinderh. **51**:1, 1909.

13. Bethe, M.: Allgemeine Anatomie und Physiologie des Nervensystem, Leipzig, C. Thieme, 1903.

the perinuclear net of Donnagio, and described a coarse pericellular or Golgi net. The dustlike granules were considered to be degenerated portions of the intracellular net, while the more resistant Golgi net only later degenerated.

Economo [14] and Bielschowsky [15] showed, however, that the endocellular net is not of neurofibrillar origin, but is part of the cytoplasmic reticulum. They demonstrated that the Golgi net was only a condensation of the diffuse glia reticulum of Held about the cells and their processes. Bielschowsky added that Schaffer's [16] resistant Golgi net in amaurotic idiocy was composed of peripherally compressed neurofibrils. It was observed that the cytoplasmic reticulum, made visible by the abnormal lipoid material, ultimately degenerates. The neurofibrils which are pushed against the cell membrane later also disintegrate.

The gross abnormalities in the convolutions of the two brains described have been found and described in detail by Schaffer [17] from his material. He found disturbances in myelogenesis, pithecoid cortical layers and embryonal fissuring, and concluded that these changes were evidence of an embryonal weakness of the ectodermal structures which predisposed to the disease process. He considered that the essential pathologic condition was an initial swelling of the cell hyaloplasm with subsequent lipoidal degenerative changes.

Bielschowsky, however, found intracellular lipoids without much swelling of the cells, and concluded that Schaffer's theory was faulty. He believed that the lipoidal change was a disturbance in the vegetative function of the cell.[18] Mott [19] believed that there was a deficiency of

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14. Economo, C.: Zur normalen Anatomie der Ganglienzellen, Arch. f. Psychiat. **41**:158, 1906.

15. Bielschowsky, M.: Ueber die fibrilläre Strukture der Ganglienzellen, J. f. Psychol. u. Neurol. **10**:274, 1908.

16. Schaffer, K.: Das Verhalten der fibrillo-retikulären Substanz bei Schwellungen der Nervenzellen, Neurol. Centralbl. **25**:834, 1906.

17. Schaffer, K.: Neue Beiträge zur Mikromorphologie und anatomischer Characterisierung der infantile amaurotische Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **46**:1, 1919.

18. L. Pick (Der Morbus gaucher and die ihm ähnlichen Erkrankungen, die lipoid zellige Splenohepatomegalie, Typus Niemann, Ergebn. d. inn. Med. u. Kinderh. **29**:519, 1926) noted the association in one case of splenomegaly type Niemann with lipoid within the ganglion cells. This lipoid was of the same chemical nature as that within the splenic foam cells. Knox, Wahl and Schmeisser (Gaucher's Disease: A Report of Two Cases in Infants, Bull. Johns Hopkins Hosp. **27**:1, 1916) report a case belonging to Niemann's type of splenomegaly apparently associated with amaurotic idiocy. W. Bloom (Splenomegaly Type Gaucher and Lipoid Histiocytosis Type Niemann, Am. J. Path. **1**:595, 1925) found that five of the seven reported cases of Niemann's disease were in Jews. In his cases the lipoid content of the splenic foam cells

nucleoproteins and that the nucleus provided a splitting ferment but not a synthetic enzyme to convert the lipoids to simpler substances. Gordon [20] and Savini [21] considered an endocrine disturbance the basis of the pathologic change.

Hassin [10] found well preserved Nissl bodies about the nucleus, as did Vogt,[12] in cells which had not reached their terminal stage, and believed the fundamental process to be an agenesis of Nissl substance, with secondary degenerative changes. His theory cannot be corroborated by this study.

The cases reported here revealed very early changes. The initial nuclear swelling and hyperchromatic appearance, the development of lipoid at the base of normally sized cells which contained their full quota of Nissl bodies and normal neurofibrils and the gradual invasion of the cells by lipoids were the earliest pathologic abnormalities. Later the visible cytoplasmic reticulum degenerated, and still later the intracellular neurofibrils. The cell swelling was a secondary matter and apparently was a result of distention by the lipoids.

The fact that normal cells may be seen late in the course of the disease and that transition stages to the final disintegration of the cell can still be seen, gives rise to the belief that the brains, although they contain gross developmental defects, were composed of morphologically normal cells at birth.

Retinal Changes.—The first studies of the retinal lesions by Mohr,[22] Frank [23] and Kingdon and Russel [24] gave the impression, because of the wide interganglionic spaces, that there was only an edema of the gangli-

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was identical with that found by me in the ganglion cells of amaurotic idiocy. The brain from Bloom's case *C* was available to me for study. Added to a pneumococcic meningitis the ganglion cells were swollen and distended with vacuoles, the chemical nature of which could not be determined because ot lengthy fixation in museum fluid. The histologic appearance, however, was that of the early cell type seen in amaurotic idiocy. These three cases suggest the possibility that a generalized disturbance of lipoid metabolism may play a part in the pathogenesis of amaurotic idiocy.

19. Mott, F., and Carlyll, H.: Seven Cases of Amaurotic Idiocy, Arch. Neurol. **3**:218, 1907.

20. Gordon, A.: Cases Allied to Amaurotic Family Idiocy with Remarks on the Pathogenesis of the Affection, New York M. J. **85**:294, 1907.

21. Savini, C., and Savini, E.: Beitrag zur Aetiologie, Pathogenese und pathologische Anatomie der Tay Sachs'schen familiäre amaurotische Idiotie, Ztschr. f. Kinderh. **7**:321, 1913.

22. Mohr, M.: Die Sachs'sche amaurotische familiäre Idiotie, Arch. f. Augenh. **41**:285, 1900.

23. Frank, Mortimer: A Case of Amaurotic Family Idiocy, J. A. M. A. **46**:187 (Jan. 20) 1906.

24. Kingdon, E., and Russel, R.: Infantile Cerebral Degeneration with Symmetrical Changes at the Macula, Medico-Chir. Tr., Edinburgh **80**:87, 1897.

onic internuclear layers. This appearance is now known to be a result in part of the loss of degenerated cells. Verhoeff,[25] Hancock and Coats,[26] and Çohen and Dixon [27] have described the retinal changes in detail, which are in accord with the changes in the retinas described previously. The ganglion cells undergo the same process as the cortical cells. They become swollen and have a reticular cytoplasm containing lipoid, which stains bright blue with hematoxylin. Later, the cells disintegrate and are replaced by fibrous glia.

In the infantile type no other retinal layer than the ganglionic and internuclear is affected, but as shown by Bielschowsky,[28] Stock [29] and Greenfield and Holmes,[9] in the juvenile type the outer nuclear layer is profoundly degenerated and is replaced by proliferated glia. The pigment layer is also definitely increased, invading the degenerated outer nuclear layer. On the other hand, cases in adults, which reveal in the brain the typical cell changes, may progress without retinal lesions, as was described by Schob [30] and Walter.[31] There does not seem to be any uniformity in the retinal pathologic condition in the various types of the disease, or any graded severity.

Lipoids.[32]—Wolfsohn and Oliver [33] described an orange red material in scharlach preparations within the ganglion cells containing doubly

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25. Verhoeff, F.: Amaurotic Idiocy: Histological Examination of a Case in Which the Eyes Were Removed Immediately After Death, Arch. Ophth. **38**:107, 1909.

26. Hancock, W., and Coats, G.: Pathological Examination of Freshly Fixed Eyes from a Case of Amaurotic Family Idiocy, Brain **33**:514, 1911.

27. Cohen, Martin; and Dixon, G. S.: Report of a Case of Amaurotic Family Idiocy, J. A. M. A. **48**:1751 (May 25) 1907.

28. Bielschowsky, M.: Zur Histopathologie und Pathogenese der amaurotischen Idiotie mit besonderer Berücksichtingung der zerebellaren Veränderungen, J. f. Psychol. u. Neurol. **26**:123, 1920.

29. Stock, W.: Ueber eine bis jetzt noch nicht beschriebene Form der familiär auftretende Netzhaut Degeneration bei gleichzeitiger Verblödung und über typische Pigment Degeneration der Netzhaut, Klin. Monatsbl. f. Augenh. **24**:51, 1908.

30. Schob, F.: Zur pathologische Anatomie der juvenilen Form der amaurotische Idiotie, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:303, 1912.

31. Walter, F. K.: Ueber "familiäre Idiotie," Ztschr. f. d. ges. Neurol. u. Psychiat. **40**:349, 1918.

32. T. von Lehoczky (Beitrage zur Histopathologie der lecithinoiden Degeneration, Virchows Arch. f. path. Anat. **261**:516, 1926) found the same lipoid material in the ganglion cells and encrusted on the golgi net as is usually found in amaurotic idioocy, in a case of tuberculous meningitis. He believes that the presence of this lipoid signifies a definite type of degeneration which is endogenous in origin in amaurotic idiocy but which may result from exogenous factors.

33. Wolfsohn, J. M., and Oliver, J. R.: Amaurotic Idiocy, General and Historical Consideration with Report of a Case, Arch. Int. Med. **16**:257 (Aug.) 1915.

refractile globules. In the glia and adventitial cells they found bright red droplets. Although they did not use differential methods, they concluded that the intracellular lipoid was a mixture of phosphatids and cholesterol esters which was gradually broken down from its complex form into simpler components by the glia and adventitial cells.

Schaffer [34] classified amaurotic idiocy according to the staining reactions of the intracellular substance. The infantile type contained prelipoid material which took a hematoxylin stain, the juvenile type stained well with scharlach R and the adult type with osmic acid. He considered that all three types underwent the same process, the composition of the lipoid material becoming simpler with duration of the disease.

Hurst,[4] in his studies of the lipoids in various neuronic degenerations, concluded that the infantile and juvenile types varied only in their lipoid content. In his infantile cases there were readily soluble phosphatids and cerebrosides, while in his juvenile case the same lipoidal mixture did not take a hematoxylin stain and was difficultly soluble in all fat solvents. He thus found a gradual transition of the lipoid to the senile lipochrome pigment, which is insoluble in all reagents.

This study has yielded results similar to those of Hurst. The intracellular lipoid, with the exception of its resistance to complete solubility, reacted the same as normal myelin. Some readily soluble neutral fat was found in the gitter cells. A few doubly refractile crystals were found which were readily soluble in acetone. The remainder of the lipoid mass reacted as phosphatids and cerebrosides, but was never completely soluble in any reagent. Even in the process of celloidin embedding a bright golden pigment was still visible, as it was after hot xylol treatment. Hurst found the same atypical solubility and concluded that it was due to a lipoprotein combination.

If Schaffer's [8] theory that the initial process is a swelling of the hyaloplasm resulting in the precipitation of the intracellular lipoids is correct, then according to the physical property of emulsions the entire lipoid material in the cell should precipitate out of its emulsion at once. However, the early cell changes which have been described demonstrate that the lipoid material appears first locally at the base of the cell and then gradually increases in amount.

Little of the lipoid material is converted into a simpler fat; in only relatively few glia cells was neutral fat found. The resemblance of the lipoid in the glia to that in the ganglion cells does not necessarily mean that the glia has suffered the same type of degeneration and that the disease therefore affects the entire nervous ectoderm. The lipoid containing glia cells are perineural in position and apparently have absorbed

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34. Schaffer, K.: Tatsächliches und Hypothetisches aus der Histopathologie der infantile amaurotische Idiotie, Arch. f. Psychiat. **64**:570, 1922.

some of the ganglion cell contents. Their nuclei show signs of having reacted for the occasion.

Apparently, the lipoid is difficultly disposed of, just as is the case with the normal lipochrome pigment. In other types of neuronic degeneration Hurst finds that the phosphatid, cholesterol and cerebroside combination separates into its components and is readily converted into fatty acids and then quickly into neutral fat. In amaurotic idiocy, therefore, some strong combination with the lipoids must exist which prevents their conversion into neutral fat. The atypical solubility, and the resemblance to the lipochrome pigment or "Abnutzungs Pigment" which is an accompaniment of senile changes within the cell, suggest a composition of the intracellular material in amaurotic idiocy, similar to that of senile lipochrome.

The gradual development in a brain with congenital defects of a slowly increasing amount of intracellular pigment resembling senile pigment makes it more than likely that the process is a premature senile change in the cell. This may be due to a faulty cellular metabolism, a disturbance in its vegetative functions, a generalized disturbance in lipid metabolism, an endocrine disorder or the presence of abnormal ferments. None of these can be demonstrated, and the microscopic picture may be identical. It is probable that primarily the cells are of normal morphology, and that after a variable period of apparently normal functioning they undergo a pathologic process similar in its slowness and ultimate lipoid product to senility. Microscopic studies do not lead us far toward a knowledge of the pathogenesis of amaurotic idiocy. What may be suggested at most is that the process, because of the similarity of its successive stages to those which occur in senility, is one of precocious senility or presenility, so far as the chemical and morphologic changes within the ganglion cells are concerned, an abiotrophy, in the sense of Gowers.

SUMMARY

Studies of the microscopic anatomy were made in two amaurotic idiots. Developmental abnormalities were described in the configuration and size of the convolutions, the presence of a fetal cord sulcus and a thin granular layer of one cerebellum.

Ganglion cells of normal size and shape were seen, with apparent transitional stages to the characteristic large swollen pear-shaped cells.

The process was a gradual replacement of the cell substance by a lipoid material, at first appearing between normal Nissl bodies; increasing in amount, it was contained in a cytoplasmic reticulum, which later disintegrated.

The retinas revealed a severe alteration in the ganglon cell layer; the other layers were entirely normal.

A differential study of the lipoids classified them, save for a small amount of neutral fat in the gitter cells, as mixtures of cholesterol, phosphatids and cerebrosides, which were atypical in that they were not completely soluble in any lipoid solvent.

Thus, the lipoids resembled senile lipochrome pigment. This resemblance and the gradual accumulation of lipoids in apparently morphologically normal cells suggest a similarity of the process to cellular presenility.

DYNAMICS OF HISTOGENESIS IN CARDIAC REPAIR

THE RÔLE PLAYED BY CONNECTIVE TISSUE *

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AND
ADAM M. MILLER, A.M.
BROOKLYN

The study of cardiac hypertrophy and atrophy has been directed chiefly on the changes that occur in the muscle. Many of the older writers, Vogl,[1] Kollicker,[2] Orth,[3] Hyrtl,[4] Rokitansky,[5] Wideroe[6] and others, held the opinion that hypertrophy was due to the multiplication of muscle fibers. Wedl,[7] Foerster,[8] Friedrich,[9] Paget,[10] Adami[11] and many others maintained that there was an increase in the size of the fibers as well as in the number. The most recent workers, Karsner, Saphir and Todd,[12] maintain that in cardiac hypertrophy the increase is due to hypertrophy of the individual fibers and that there is no increase in number. These later investigators also hold that in atrophy there is a decrease in the number of fibers as well as a reduction in the size of the individual fibers. Thus, extensive observations have been made on the cardiac muscle, but the changes which take place in the connective tissue that constitutes a part of the heart wall seem to have received scant attention.

It is our object in this article to consider the connective tissue of the heart, particularly the elastic tissue, and to offer an explanation of the

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* From the Department of Anatomy, the Long Island College Hospital.

1. Vogl, J.: Pathologische Anatomie, Leipzig, L. Voss, 1854.

2. Kollicker, A.: Handbuch der Gewebelehre, Leipzig, W. Engelmann, 1852.

3. Orth, J.: Lehrbuch der speciellen pathologischen Anatomie, Berlin, A. Hirschwald, 1887.

4. Hyrtl, quoted by Karsner, Saphir and Todd (footnote 12).

5. Rokitansky, von C.: Lehrbuch der pathologischen Anatomie, Vienna, W. Braumüller, 1856.

6. Wideroe, S.: Histologische Studien uber die Muskulatur des Herzens, Virchow's Arch. f. path. Anat. **204**:190, 1911.

7. Wedl, quoted by Karsner, Saphir and Todd (footnote 12).

8. Foerster, A.: Handbuch der speciellen pathologischen Anatomie, Leipzig, L. Voss, 1852.

9. Friedrich, N.: Krankheiten des Herzens, Virchow's Handbuch der speciellen Pathologie und Therapie, Erlangen, F. Enke, 1861.

10. Paget, J.: Lectures on Surgical Pathology, Philadelphia, Lindsay and Blakiston, 1865.

11. Adami, quoted by Karsner, Saphir and Todd (footnote 12).

12. Karsner, Saphir and Todd: The Cardiac Muscle in Hypertrophy and Atrophy, Am. J. Path. **1**:351, 1925.

changes observed in relation to cardiac repair. In a separate article we have described the amount and distribution of elastic tissue found in the presumably normal heart at different ages. The outstanding feature of those observations was the gradual increase of the elastic tissue from infancy to old age. This was such a constant observation that after an examination of a large series of hearts, in which differential stains were used to bring out the elastic tissue, the age of a given normal heart could be pretty accurately judged from the relative amount of elastic tissue observed in various parts of the heart wall. While studying the large series from which the normal hearts were chosen, a great many hearts showing abnormal changes were also encountered. It was observed in the latter that when elastic tissue was present in excess of the age norm, invariably there were other pathologic conditions in the cardiac structures, or reports of pathologic observations in other organs, or there had been histories and physical signs which indicated changes elsewhere. It seemed that in many, if not all, of these cases the elastic tissue was an expression of an effort by the heart to meet and overcome added resistance to its customary activity. On this ground we have made a further study of many hearts which exhibited marked connective tissue, and especially elastic tissue, changes.

The material that was studied comprised nearly 100 hearts, normal and pathologic. The majority of the hearts in our series showed definite pathologic changes or conditions, which in our opinion reflected an attempt by the organ to adjust its mechanism to abnormal or pathologic states elsewhere in the body. Sections were stained with hematoxylin and eosin, with Mallory's stain for collagenous fibers, with Verhoeff's elastic tissue stain and with Weigert's elastic tissue stain. The last two yielded excellent results with our material, the Weigert preparations usually being the clearer. We accepted the proposition that both of these mixtures were specific for elastic tissue. The areas illustrated are representative for the hearts in question and the description is applicable in general; in other words, the figures and description are not merely those of changes which might be of a purely local nature.

Old age does not necessarily mean extensive change in the heart muscle, as the heart may be comparatively healthy and vigorous. Pathologists seem generally to maintain that atrophy is not as common in the heart as in some other organs of the body. This relative infrequency of atrophic changes in the hearts of old age, granting that they have not been subjected to various tissue insults, may be explained on the basis of continuous work. The organ as a whole, as well as all of its separate parts, does not have an opportunity to become sluggish through inactivity, or atrophic through disuse.

Atrophy of the heart in old age is generally accompanied by degenerative changes in the vascular system of the entire body. With these degenerative changes, the heart is compelled to do more work in order to overcome the added resistance. The first response to the additional burden is hypertrophy, which then exists until the heart muscle becomes exhausted. After hypertrophy and exhaustion, atrophy sets in. The

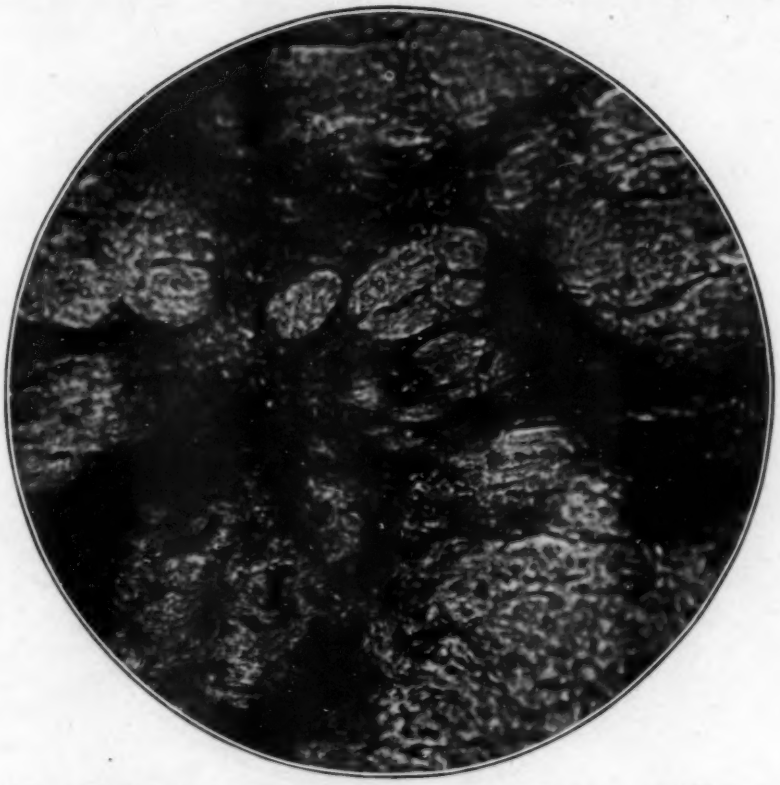

Fig. 1.—Section of ventricular myocardium showing fragments of degenerating muscle in the center of the scar tissue which is almost entirely made up of elastic tissue. × 160.

histologic picture obtained in atrophy depends on the nutritive capacity and blood supply of the cardiac muscle.

In a heart in which the nutritive supply has been diminished so-called "fibrosis" is found. An increase in connective tissue occurs in definite localities in the following order: endocardium, pericardium, perimysium, septums extending into the muscular fasculi. The endomysium is increased generally, and where degenerating muscle fibers are found, there are large islands of connective tissue. At times, fragments of the

degenerating muscle fibers are seen in the center of the connective tissue island (fig. 1).

Our studies have shown that the increase of connective tissue is in proportion to the degeneration of muscle tissue in those hearts in which, judging from conditions in general, the degeneration has been a slow, progressive change. In some regions the reformed connective tissue was composed principally of collagenous fibers. But in other regions there were all the intermediate stages between the collagenous fibers

Fig. 2.—Section of endocardium from the left auricle of a man, aged 60, in which there was not any evidence of change in the myocardium. × 160.

which did not take any of the elastic tissue stain and the darkly staining elastic fibers. In the large areas of connective tissue in which we might be justified in saying that this transformation had been going on for a long time, we found that in some instances the entire mass was stained with the elastic tissue dye.

The endocardium of hearts in cases of arteriosclerosis and hypertension showed a marked increase in thickness and a difference in the quality of the tissue as compared with the corresponding layer in hearts

of similar age with which definite pathologic conditions could not be associated. Figure 2 shows a section of the endocardium of the left auricle taken from a man, aged 60, in which the myocardium does not yield evidence of any morbid changes. Here may be observed the various strata of the endocardium, as described in our article on age changes. Figure 3 shows a section of endocardium from the left auricle of a man, aged 70, with a history of arteriosclerosis and hypertension over a period of years. There is a marked increase in thickness

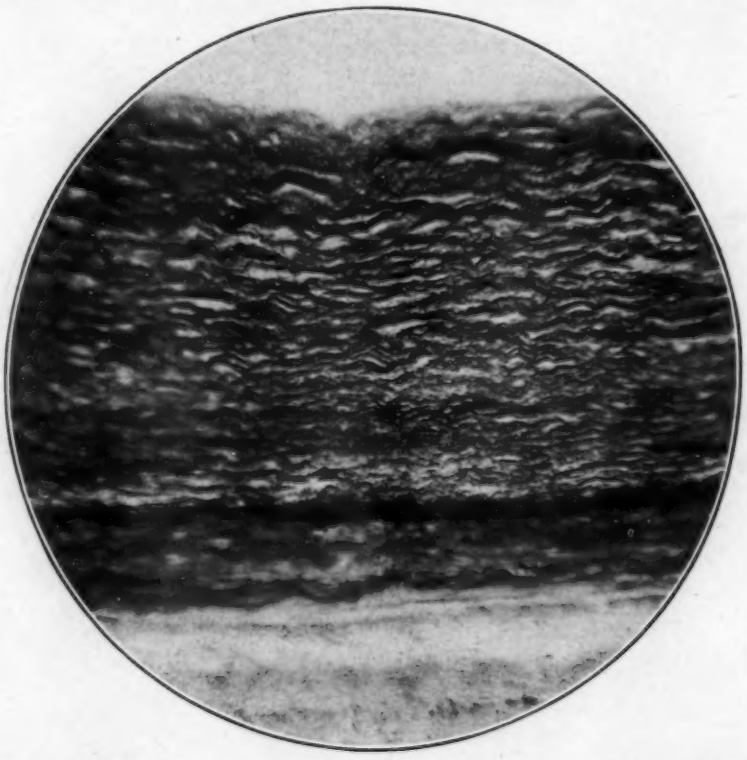

Fig. 3.—Section of endocardium from the left auricle of a man, aged 70, with a history of arteriosclerosis and hypertension for many years. × 160.

of the endocardium as well as a lack of differentiation into strata. The endocardium is made up almost entirely of tissue which takes the elastic tissue stain. The fibers vary in thickness from slender delicate threads to heavy bundles of closely packed coarse strands which have the gross appearance of collagenous fibers. As stated elsewhere, it is our opinion that these large bundles represent collagenous fibers in which the individual fibrils have changed chemically so that they react specifically to the elastic tissue stain. From this point of view they are new elastic

fibers. In the subendothelial layer (fig. 2) the smoky appearance of the collagenous fibers is marked. Under high magnification this appearance is observed to be due to dark granules in the collagenic fibers which apparently represent an early stage in this transformation.

A section of endocardium of the left auricle of a man, aged 80, is seen in figure 4. This heart showed well preserved cardiac muscle and no evidence of any morbid changes. Although twenty years older than the normal endocardium seen in figure 2, there is still a relatively

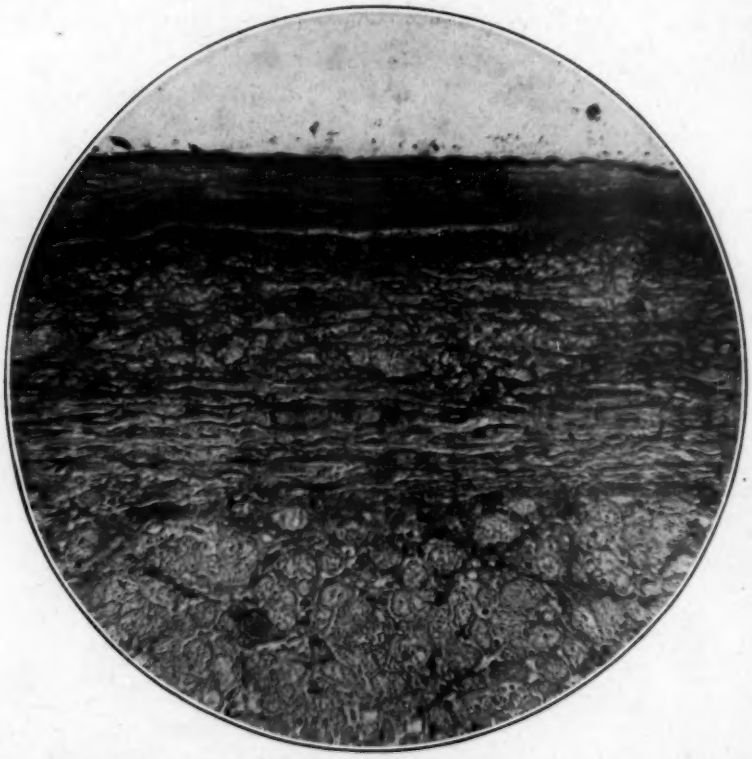

Fig. 4.—Section of endocardium from the left auricle of a man, aged 80, without evidence of cardiac disease. × 160.

small amount of elastic tissue present, as compared with pathologic hearts. Figure 5 shows a section taken from the left auricular endocardium of a man, aged 82, who had marked arteriosclerosis. The endocardium is nearly twice as thick as that in figure 4, although the heart is only two years older. The thickness is due to the presence of both collagenous and elastic tissue, although the latter is actually less in amount than that in a heart twelve years younger as shown in figure 4. A section of the left ventricle of the 82 year old heart is

Fig. 5.—Section of endocardium from the left auricle of a man, aged 82, with marked arteriosclerosis. × 160.

Fig. 6.—Section of the left ventricular myocardium from the same heart as that in figure 5. × 160.

seen in figure 6 and a section of the 70 year old ventricle in figure 7. It should be noted that the younger myocardium exhibits the greater amount of elastic tissue in the endomysium. Comparison of the case histories and autopsy observations in these two cases revealed that there had been a longer period of arteriosclerosis in the person, aged 70, than in the one, aged 82.

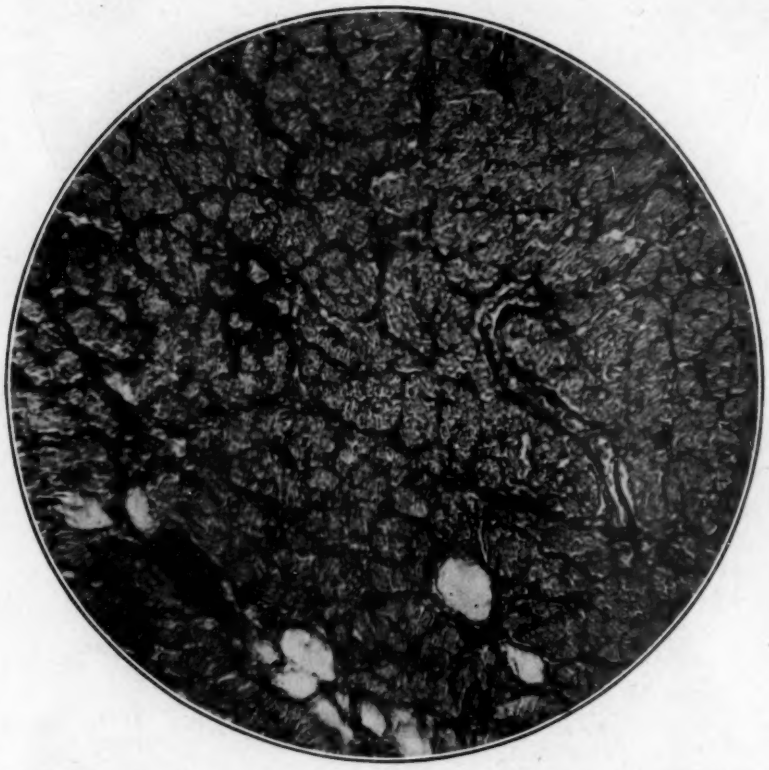

Fig. 7.—Section of the left ventricular myocardium from the same heart as that in figure 3. × 160.

This same sequence of events apparently occurs as an ordinary process of repair following acute myocarditis. When connective tissue proliferation begins, following an acute condition of this type, there is first a fibroblastic infiltration; then collagenous fibers develop, and as time goes on elastic tissue appears. In one instance the muscle tissue had completely degenerated in a small area of the auricle, and scar tissue which had replaced the muscle was made up largely of elastic tissue (fig. 8). In another instance a small thrombosed vessel was found in which complete organization of the thrombus had taken place, and the connective tissue stained deeply with the elastic tissue stain.

There are different opinions as to the reformation of elastic tissue. Beattie and Dickson [13] say that it can be reformed by "off-shoots from the pre-existing elastic fibers, possibly through the agency of cells, not yet satisfactorily demonstrated." Milne,[14] in discussing repair in other organs, believes that it is derived from some preexisting elastic tissue. Dawson [15] is of the same opinion, and further states that in scar tissue

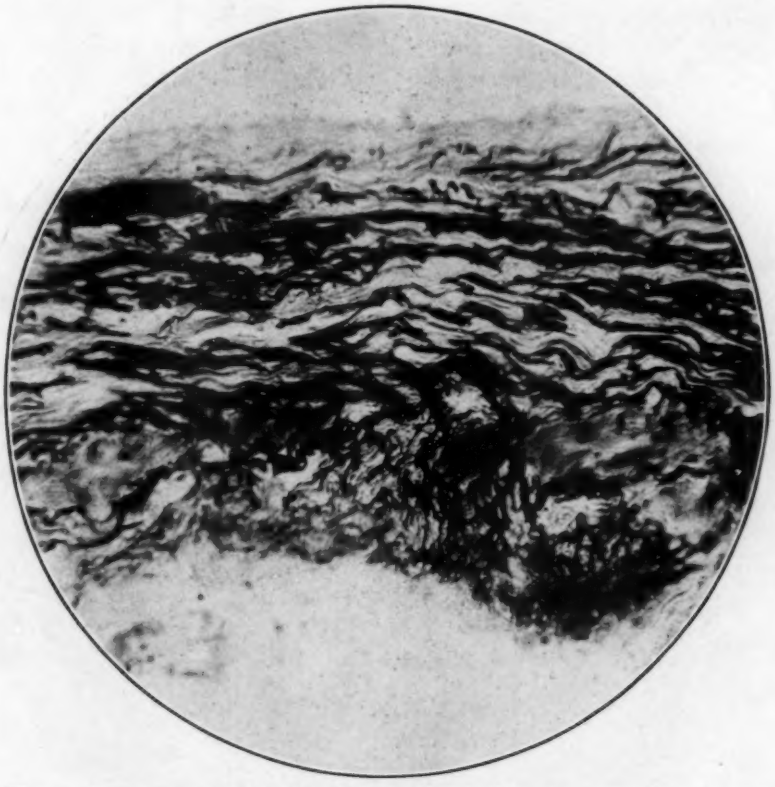

Fig. 8.—Section of left auricle in which there has been complete degeneration of muscle tissue and replacement by connective tissue rich in elastic fibers. × 160.

there is distinct evidence that elastic tissue fibers are formed from cells of the part. We conclude, from the evidence at hand, that the elastic fibers are derived directly from collagenous fibers which are so situated that they are subjected to an active existence rather than a passive one.

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13. Beattie and Dickson: General Pathology, London, W. Heinemann, ed. 3, 1925, vol. 1, p. 223.

14. Milne, quoted by Beattie and Dickson (footnote 13).

15. Dawson, quoted by Beattie and Dickson (footnote 13).

In the case of cardiac repair there are probably two factors responsible for the fibroblastic proliferation. First, there is the mechanical irritation in the atrophic heart. As the muscle fibers lose their vitality and ability to do their usual amount of work, more tension and stress are thrown on the connective tissue. As this mechanical stimulus continues to be applied in the beating heart there is a response on the part

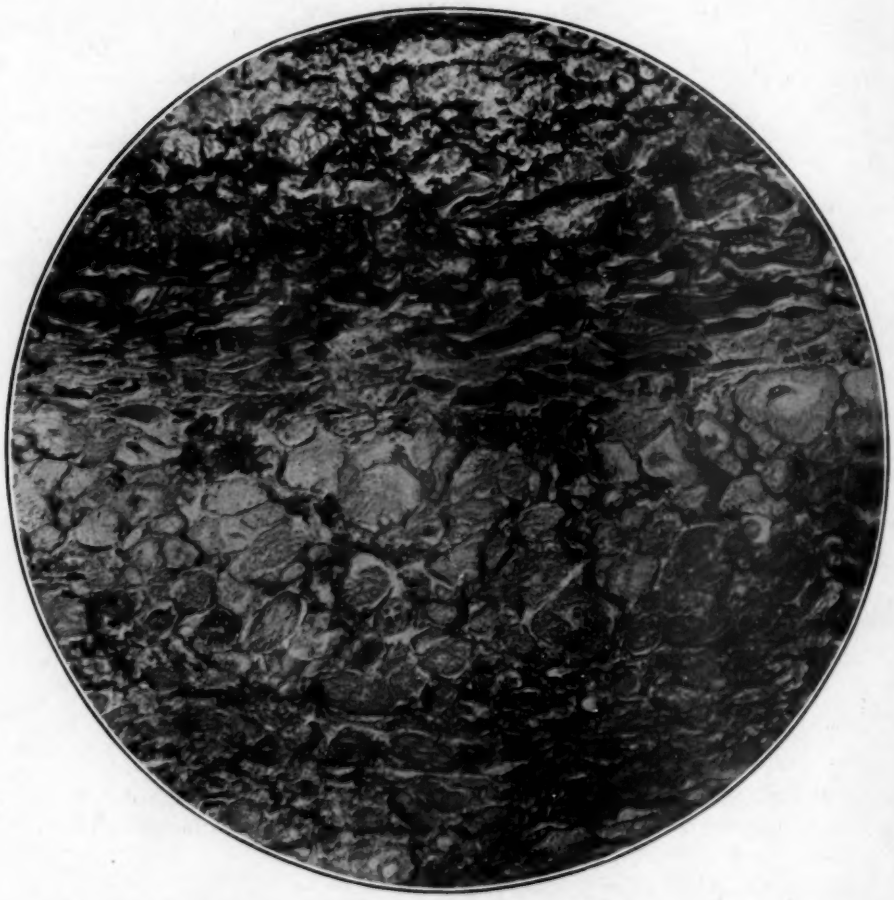

Fig. 9.—Section of myocardium of the left auricle, from a woman, aged 26, who died of acute endocarditis, showing various stages of degeneration of the muscle fibers with an increase in the endomysium but little differentiation into elastic tissue. × 160.

of the connective tissue which is expressed in an increase in fibroblasts and collagenous fibers. In the inflammatory conditions a second factor is added, that of chemical stimulation, although the ultimate result is the same. As tension and stress continue over longer periods the fibers

are changed chemically inasmuch as they differ in their reaction to specific dyes. At first they take only a slight amount of the elastic tissue stain, and then they vary in density up to darkly staining fibers having all the appearance of elastic fibers. The finer details of this transformation are reserved for future publication.

In the studies in the dynamics of histogenesis by Eben J. Carey,[16] we wish to call attention to the following statement: "The genesis, growth, maturity, and hypertrophy of muscle is a quantitative property of its function or work. The genesis, growth and hypertrophy of muscle is a direct index of an increase in the tension within definite limits. When the tension becomes relatively constant at maturity, the muscle remains relatively constant in size. With an increase in tension, after maturity is reached, there is increase in muscular work. Since muscular work equals tension times contraction, an increase in tension within certain limits leads to increased function. This in turn produces muscular hypertrophy because of the increased metabolic rate." We believe that this proposition can be applied to the conditions found in the heart. When the pressure of the blood stream is increased either through degenerative processes in the blood vessels or through pathologic changes in the kidney, more work is thrown on the myocardium. Since this is generally a gradual increase, there is a response on the part of the myocardium which is expressed in hypertrophy. Then when certain fibers are unable to carry the extra load and degenerate, the connective tissue, which has been playing a relatively passive rôle, is introduced to a new environment in which stress and tension are important factors that operate to produce more connective tissue and bring about the transformation of collagenous fibers into elastic fibers. Cannon [17] suggested that there was a subminimal, an optimum and a supermaximal tensional stimulus to elicit the response of the contractile tissue of the stomach in the normal stomachic movements. Carey found an analogy in the development of musculature. We suggest a similar analogy in the differentiation of elastic tissue.

When there is a sudden attack on the cardiac muscle resulting in degeneration, as seen in various toxic conditions, the degeneration may be too rapid to allow either of the two defensive agencies (hypertrophy of the healthy muscle or hyperplasia and differentiation of connective tissue) to appear. In such cases dilatation of the chamber is involved. If the attack is sufficiently localized or is slow in its progress then the defense mechanisms are brought into play.

In hearts which have been subjected to various types of toxemias interesting and significant pictures are presented. In a case of a woman,

16. Carey, E. J.: Anat. Record **24**:95 (Oct.) 1922.
17. Cannon, W. B.: Am. J. Physiol. **29**:255, 1911.

aged 26, who died of acute endocarditis, the left auricle was found, at autopsy, to be dilated to such an extent that the capacity was approximately four times that of a normal left auricle. There was no rheumatic or cardiac history up to five months before the time of death. The endocardium showed marked increase in collagenous tissue with con-

Fig. 10.—Section of the endocardium of the left auricle from the same heart as that in figure 11, showing increase in thickness and also in the amount of elastic tissue. × 160.

siderable increase in elastic tissue in the juxtamuscular layer. In figure 9 showing the myocardium are seen the cross sections of the muscle fibers which present different stages of degeneration, from fairly healthy fibers to those which have increased to two or three times the normal size. These large fibers are edematous and pale, and show hyaline degeneration. Fibroblastic infiltration has taken place and an increase in

collagenous fibers in the endomysium, but little differentiation into elastic tissue. The conclusion seems justified here that the pathologic picture is one of comparatively short duration, the lapse of time not having been sufficient for a reaction resulting in the extensive formation of elastic tissue.

Fig. 11.—Section of myocardium of the left auricle, from a woman, aged 23, who died of cardiac decompensation, showing an increase in the endomysial tissue with differentiation into elastic tissue. × 320.

A woman, aged 23, who died of cardiac decompensation four days after an abdominal operation, gave a history of chorea at the age of 10, rheumatism for the last eight years and a previous break in compensation two and one-half years before admission. In this case an entirely different pathologic picture was observed. The endocardium of the left auricle, presented in figure 10, might be compared to one that would be

seen in a senile heart with arteriosclerosis such as that in figure 3. It is at least twice the thickness of an ordinary endocardium at that age and shows an enormous increase in elastic tissue throughout the various layers. In the myocardium is found also an increase in endomysial tissue, but the tissue stains with the elastic tissue dyes (fig. 11). In this instance the picture is that of extensive elastic tissue formation

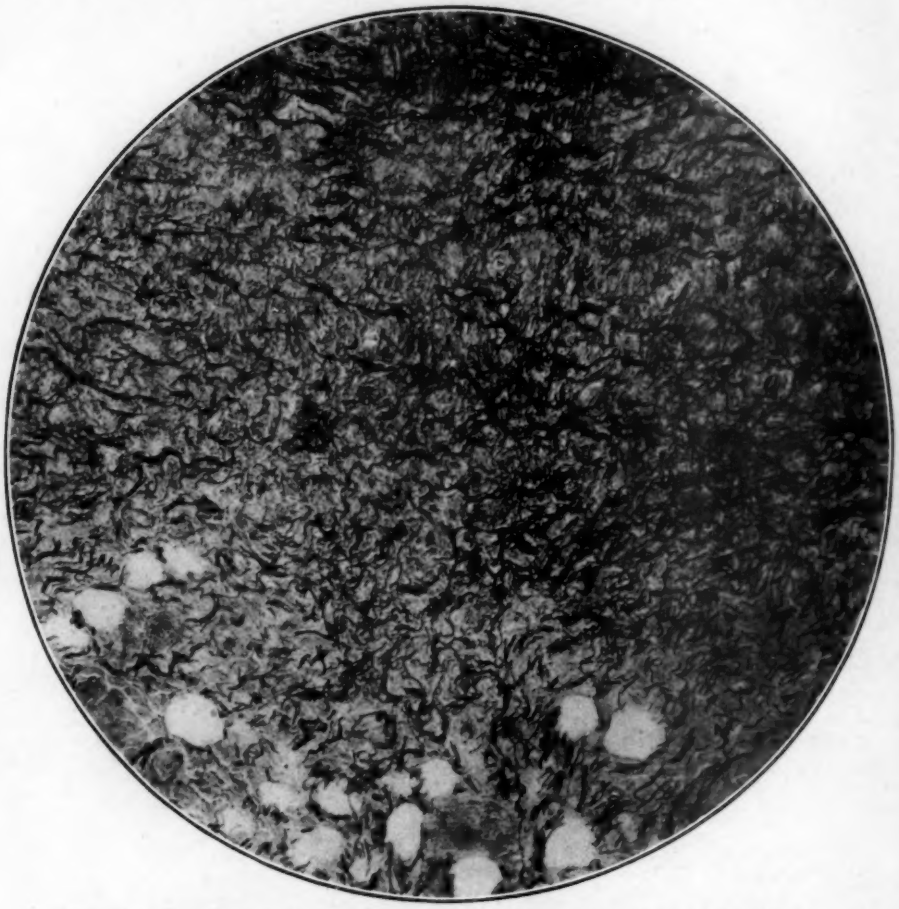

Fig. 12.—Area of degeneration of ventricular myocardium and replacement by connective tissue with differentiation into elastic tisue. × 160.

which would result from the application of stimuli over a considerable period, and the history of the case confirms this interpretation.

In certain myocardiums in which there has been marked local destruction of muscle tissue, the muscle is replaced by both collagenous and elastic fibers, the latter being rather generally distributed (fig. 12). In other instances still better defined local collections of elastic fibers extend in some plane through the scar (fig. 13). If our deductions are

correct in regard to this formation of elastic tissue we might go one step further in the explanation of the foregoing conditions: In the cases in which the elastic tissue forms in a general way throughout the scar tissue, the stress thrown on the scar may be in several planes at the time of diastole, while in the second type in which it is concentrated in one plane, this plane may represent the plane of maximum stress.

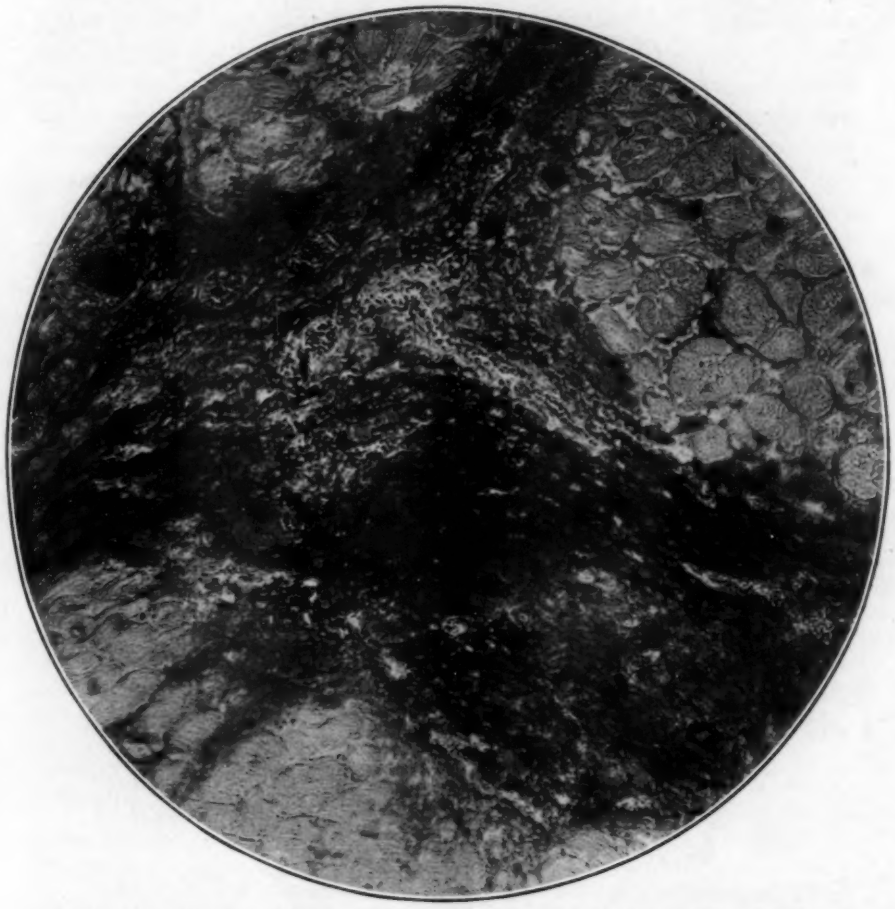

Fig. 13.—Area of cardiac repair in which the elastic tissue differentiation is limited to a definite plane, horizontal in the figure. × 160.

SUMMARY

With increasing age but without cardiac or other vascular lesions there is an increase in the amount of elastic tissue in the different layers of the heart wall. This observation will be set forth in detail in a separate publication.

In cases of arteriosclerosis in which the heart muscle is damaged as a result of nutritional disturbances, the connective tissue of the epicardium, endocardium and myocardium increases in amount, the increase being characterized by the appearance of large quantities of elastic tissue. The amount of elastic tissue appears to be directly proportional to the damage suffered by the cardiac muscle.

In toxic conditions with sudden effect on the heart, formation of elastic tissue does not occur in conjunction with the damage to the heart muscle, but in toxic conditions in which the attack on the heart muscle is prolonged, a marked development of elastic tissue takes place. The elastic tissue may be regarded as a compensatory mechanism in the heart wall when there has been slow damage to the cardiac muscle.

The evidence in our material points to the conclusion that collagenous fibers may be transformed into elastic tissue in consequence of prolonged stress and strain on the connective tissue containing the collagenous elements.

PRIMARY SCLEROSIS OF THE PULMONARY ARTERY AND ITS BRANCHES*

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Primary or genuine sclerosis of the pulmonary artery and Ayerza's disease are two clinical entities which have been studied with increasing frequency during the last twenty-five years. Even though diminution of the pulmonary artery bed by sclerosis of the pulmonary artery and its branches is the essential morbid alteration ascribed to both of these diseases, the clinical manifestations, as described by their exponents, are in many respects dissimilar. Most authors describe syphilitic arteritis of the pulmonary artery in Ayerza's disease, whereas in the other disease syphilis generally has been excluded and another single common etiologic factor has not been found.

PRIMARY SCLEROSIS OF THE PULMONARY ARTERY AND ITS BRANCHES

Posselt [1] was the first to summarize definitely the clinical characteristics of primary sclerosis of the pulmonary artery and to review its literature. Eppinger and Wagner [2] in 1920 emphasized the chief clinical manifestations in reporting five cases, in three of which the correct diagnosis was made before death. These authors collected sixteen cases, the first being by Crudeli in 1870. Posselt [3] again reviewed the literature in 1925, and again defined its clinical and anatomic features. In addition to these reports there are others by H. Schütte,[4] H. R. Miller,[5] H. Liebig,[6] O. Meyer [7] and Löwenstein.[8]

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1. Posselt, A.: Die klinische Diagnose der Pulmonalarteriosklerose, Samml. klin. Vortr., no. 504-507, 1908. Die Erkrankungen der Lungenschlagader, Ergebn. d. allg. Pathol. u. path. Anat. **13**:298, 1909.

2. Eppinger, H., and Wagner, R.: Zur Pathologie der Lunge, Wien. Arch. f. inn. Med. **1**:83-118, 1920.

3. Posselt, A.: Zur Pathologie und Klinik der primaren Atherosklerosis pulmonalis, Wien. Arch. f. inn. Med. **11**:357-398, 1925.

4. Schütte, H.: Rechtseitige Herzhypertrophie, hervorgerufen durch entzündliche Veränderung der kleinen Lungenarterien, Centralbl. f. allg. Pathol. u. path. Anat. **25**:483, 1914.

5. Miller, H. R.: Sclerosis of the Pulmonary Artery and Its Branches, M. Clin. N. Amer. **9**:670-716, 1925.

Morbid Anatomy.—The most conspicuous gross change found at postmortem examinations is hypertrophy of the wall of the right ventricle, unassociated with the cardiac and pulmonary diseases [9] that are known to obstruct the pulmonary circulation. Death is usually caused by cardiac decompensation, with edema and marked alterations of the liver, spleen and kidneys, due to long continued passive hyperemia. The lungs are relatively bloodless and small. The wall of the left ventricle is atrophied, and the cavity of the left auricle is small. The gross alterations in the intima of the main portions of the pulmonary artery, mainly fatty change and its sequences, are usually slight in comparison to the changes in the pulmonary arterioles. Tortuosity of the smaller arteries (from 1 to 3 mm. in diameter) has been observed. The pulmonary veins are usually unaltered, but in some instances they are smaller than normal (Hart,[10] Watjen [11] and Posselt).

Microscopic examination of the lungs reveals the cause of the hypertrophy of the wall of the right ventricle, a marked lessening of the channels of the arterioles and small arteries throughout both lungs. Within the middle muscular and subintimal coats there are thick layers of fibrous tissue and usually retrogressive changes, such as hyaline degeneration, vacuolization and lipoid deposits. In the arterioles the elastic tissue of the intima is sparse, but in the arteries with a diameter greater than 0.5 mm. there are varying degrees of hyperplasia of the elastic tissue. Schütte [4] and Löwenstein [8] found extensive round cell infiltrations in the arterial walls, but in most instances inflammatory changes are not observed.

Clinical Symptoms.—The patients present the problem of determining the cause for enlargement of the right side of the heart. Mitral stenosis has been the most common diagnosis. Cyanosis is generally present and more marked than is consistent with other signs of myo-

6. Liebig, H.: Ueber die primäre Pulmonalsklerose, Zentralbl. f. Herzkrankh. **18**:45-56, 1926.

7. Meyer, O.: Zwei Fälle von Pulmonalsklerose, München. med. Wchnschr. **72**:1948, 1925.

8. Löwenstein, L.: Ueber Thromboarteriitis pulmonalis, Frankfurt. Ztschr. f. Path. **27**:226-236, 1922.

9. The usual or known causes for hypertrophy of the wall of the right ventricle are hypertrophic emphysema of the lungs, mitral stenosis and other valvular and myocardial diseases of the left side of the heart, extensive obliteration of the pleural cavities by fibrous adhesions, fibroid tuberculosis of the lungs, pneumoconiosis, chronic bronchitis and compensatory emphysema (when bronchial asthma existed during life), extensive bronchiectasis, deformities of the thoracic wall and congenital malformations of the pulmonary artery and its orifice.

10. Hart: Ueber die isolierte Sklerose der Pulmonalarterie, Berl. klin. Wchnschr. **12**:304, 1916.

11. Watjen: Isolierte Sklerose der Pulmonalarterie im jüngsten Kindesalter, Deutsche med. Wchnschr. **22**:713, 1924.

cardial insufficiency, especially shortness of breath. Edema, although it usually appears late in the disease, is more prominent than shortness of breath. Other characteristics described by Posselt and Eppinger and Wagner are as follows: the lung fields in roentgenograms are clear, and the outline of the left auricle indicates that this cavity is not enlarged; physical or roentgen-ray examinations do not reveal evidence of an adequate cause for enlargement of the right side of the heart; the systolic and pulse pressures are usually low, and the second pulmonic sound is accentuated. Posselt believes the noteworthy features possess the following order of importance: cyanosis; hypertrophy of the walls of the right heart chambers; small left auricle; absence of evidence of passive hyperemia of the lungs, and disproportion between the cyanosis and dyspnea. The disease is one of early adult life or early middle age.

AYERZA'S DISEASE

The second disease attributed to sclerosis of the pulmonary artery is named after Abel Ayerza, who described it in 1901 as "cardiacos negros." Arrillaga,[12] an associate of Ayerza, continued its study and, with others,[13] has described the clinical and anatomic characteristics. Its main features are polycythemia, marked cyanosis and hypertrophy of the wall of the right ventricle.

Morbid Anatomy.—With the hypertrophy of the wall of the right ventricle there is dilatation of the pulmonary artery in its first portion and main branches, with frequently a true aneurysm near the bifurcation and plaques in the main branches and middle-sized arteries. In the main branches there is hyperplasia of the elastic fibers in the media. In the medium-sized branches there is a panarteritis with intense reaction in the intima. The most marked changes in the smaller branches are in the media, where there is splitting of the elastic fibers and hyperplasia of the internal elastic membrane. Many of the patients have had a clinical history of bronchitis and pneumonia. Arrillaga maintains that histologic evidence of syphilitic bronchitis and pneumonia is present in some bodies, and in others, that there are bands of fibrous tissue in the lungs that increase proportionately as the arteritis diminishes the lumens.

Clinical Features.—Dyspnea is always marked and exists for a long time before symptoms of myocardial insufficiency develop. Cyanosis

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12. Arrillaga, F. C.: Early Diagnosis of Pulmonary Arteritis, Rev. Soc. de med. int. **1**:478-483, 1925. Arrillaga, Tobias and Cabred: Sclerose de l'artere pulmonaire, Rev. Asoc. med. argent. **37**:100-113, 1924.

13. Escudero, P.: Polycythemia and Erythrosis with Sclerosis of the Pulmonary Artery, Rev. Soc. de med. int. **1**:463-470, 1925. Ayerza, L.: Ayerza's Disease, Rev. Soc. de med. int. **6**:73-83, 1925. Warthin, A. S.: A Case of Ayerza's Disease, Tr. A. Am. Phys. **34**:219-239, 1919.

is so characteristic that the disease was first named "black cardiacs." Polycythemia is usually present. Death is preceded by edema and passive hyperemia of the lungs, rupture of the pulmonary artery, thrombosis or bronchopneumonia.

Arrillaga [13] maintains that sclerosis of the pulmonary artery may be diagnosed even when complicated by emphysema, chronic bronchitis, bronchiectasis and mitral stenosis. He believes that the sclerosis of the pulmonary arteries is always primary and syphilitic, and that it may be complicated by the mentioned pulmonary and valvular diseases, the latter only predisposing the arteries to the syphilitic inflammation.

Warthin [14] emphasized polycythemia in his report, and suggests that many of the forms of polycythemia reported in the literature may be due to sclerosis of the pulmonary artery. He supports the views of Arrillaga and Escudero regarding the syphilitic nature of the changes in the pulmonary artery and accepts Ayerza's disease as a clinical and anatomic entity. He also states in regard to the etiology that: "the lesions in the pulmonary vessels may be secondary to chronic pulmonary disease, bronchitis, tuberculosis, pleural adhesions or any condition producing a final emphysema; or it may be the result of slow infections, as syphilis or malaria, or the result of intoxications."

The case we will report resembles the disease described by Posselt and Eppinger and Wagner, and differs in many clinical and anatomic features from Ayerza's disease. We, therefore, have chosen the name employed by Posselt, namely, primary sclerosis of the pulmonary artery.

REPORT OF CASE

Clinical History.—M. K., a woman, aged 40, married, entered the Presbyterian Hospital, Chicago, Aug. 17, 1926, as a patient of Dr. Charles M. Bacon, complaining of shortness of breath, pain in the chest, loss of weight and a nonproductive cough. She thought that her illness followed an acute pulmonary infection in 1918, during the influenza epidemic. Until 1921, loss of weight and strength prevailed, but then shortness of breath began to appear at intervals. During February, March and April of 1922, there was thoracic pain on exertion severe enough that the patient "would have to stop walking." In 1922 there were: relative dulness in the right posterior axillary line from the fifth to the tenth ribs with diminished breath sounds; diminished breath sounds close to the spine on the left side from the fourth to the sixth ribs; no enlargement of the heart to the left; no murmurs; the first sound at the apex sharp and ringing; the hemoglobin content, 70 per cent; red blood cells, 3,980,000; white blood cells, 4,500. A roentgenogram demonstrated enlargement of the heart to the right and calcification in the lung fields. The heart beat after exertion was 100 per minute, three minutes later 100. Digitalis gave some relief. A trace of albumin was found in the urine. The weight was 98 pounds (44.5 Kg.). At this time a tentative diagnosis of pulmonary tuberculosis was made.

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14. Warthin (footnote 13, third reference).

In March, 1925, the patient weighed 99 pounds (45 Kg.); the heart rate was 90, the respiratory symptoms were improved; the hemoglobin content was 78 per cent; red blood cells, 4,610,000; white blood cells, 4,500.

During the summer of 1925, she was hardly strong enough to walk. The cough, intermittent before and nonproductive, was now paroxysmal and exhausting, with a mucopurulent yellow sputum.

From questions at the time of admission it was evident that there had been cyanosis of the fingers and feet for five years, and that recently the hands "became blue whenever they hung down." For the last year she had also noticed abdominal distress which occurred immediately after eating solid food and which was relieved by belching; vomiting, diarrhea, constipation, hemoptysis or melena had not been present, but excessive flatus had been noted. In January, 1926, swelling of the feet occurred for the first time; for four months it receded and returned several times, but during the last four months before examination it was constant. The cramplike pain in the chest was absent from 1922 to 1926. The only neurologic disturbances were four attacks of headache, each lasting about three days, localized to the right eye and temple and associated with nausea and insomnia.

The patient had been married for twenty-five years, but had never been pregnant. Menstruation was regular, with a twenty-six day interval and a duration of six days, until March, 1926, when the flow decreased and then ceased in June.

There was a severe attack of rheumatic fever during the eighth year but no recurrence. During the last several years she had "rheumatic pains" in various joints intermittently, unassociated with swelling or heat. A goiter developed at puberty, but disappeared in four years. A history of childhood or venereal diseases was not obtained. Her father was living and well; her mother had died at the age of 45 of apoplexy; two brothers were living and well. The patient did not use alcohol, tobacco, coffee or tea.

Report was made as follows after physical examination on Aug. 17, 1926: "Patient is thin, middle-aged, slightly dyspnoeic, and the lips are blue. Hearing is normal. There is no nasal obstruction or puffiness of the eyelids. The sclerae and conjunctivae are unchanged. The pupils react to light and accommodation. The tongue is rough, deeply furrowed and red. There is slight pyorrhea at the upper incisors. The pharynx and tonsils are not acutely inflamed. The thyroid gland is not enlarged. There are a few palpable lymph glands in the anterior cervical chain. The large vessels have no visible pulsations.

"The chest is thin, symmetrical in front. There is slight dorsal scoliosis. Expansion of the chest is fairly good, but excursion at bases only 2 cm. The chest is slightly hyperresonant. There are no abnormal breath sounds or dulness. The apex beat is barely felt, not localized and 100 per minute. The right heart border is 1 cm. beyond the sternal border in the fourth interspace, the left heart border 8.5 cm. from the midsternal line in the fourth and fifth interspaces. The heart tones are clear, the second tone at the left sternal margin at the base is split, the first sound at the apex rough. There is a systolic murmur heard at the lower border of the heart from the apex to the xyphoid process, loudest at the xyphoid. There are no irregularities. Blood pressure is 105 systolic and 60 diastolic in the sitting position.

"The abdomen is symmetrical and somewhat doughy. There is moderate tenderness in the epigastrium and left hypochondrium. The liver margin is 3 cm. below the costal margin in the right mid-clavicular line. The spleen is not palpable.

"There is edema of the subcutaneous tissues of the legs as high as the knees. There are a few varicose veins. The fingers are not clubbed. When the hands hang down, the fingers become deeply cyanosed.

"The vaginal canal is narrow and short. The body of the uterus is not palpable. A firm mass is palpated through the posterior fornix.

"August 19. The radial pulse is regular, 100 per minute, and small volume. The hands and feet are cold. There is tenderness in the epigastrium and resistance to firm pressure (liver). The edema is diminished.

"August 22. There are coughing spells with pain in the lower part of the chest. Fine crepitant inspiratory râles are heard at the bases. Edema of legs has almost disappeared.

"August 25. There is pain between shoulder blades, lumbar region and lower end of sternum. The lungs are clear. The temperature reached 101 F. No change found in cardiac findings."

During the last two days before death she continued to complain of pain between shoulders; cyanosis increased. Death was rather sudden, with nausea, faintness and cyanosis preceding it a few hours.

On August 17 the hemoglobin content was 85 per cent (Dare); red blood cells, 6,080,000; white blood cells, 7,000. The urine contained a slight amount of serum albumin in all tests; occasional hyaline casts were found; red blood cells were not present; the specific gravity was between 1.008 and 1.015. The blood urea nitrogen was 17.7 mg. per hundred cubic centimeters, creatinine 1.34. Blood was not found in the stools. A Wassermann test was not made.

The temperature was subnormal except on August 25 and 26, when it reached 102 F.

Electrocardiogram: "Rate 100; right heart preponderance; no arhythmia; T-wave inverted in leads II and III (the latter attributed to overdigitalization or myocardial degeneration)."

On August 20, Dr. E. E. Irons made the following observations in addition to confirming those previously mentioned: "maximum left heart border 10 cm. from midsternal line; spleen not palpable; no pulsations in liver; heart dulness shifts on change of position of patient; no thrill palpable at apex; systolic murmur at the apex and to the left of it, and over lower end of sternum a systolic murmur of like character; a short presystolic rough murmur at apex terminating in a sharp first sound; pulmonic second much accentuated; lung resonance and breath sounds are normal; color of patient this morning is normal; pulse regular, but very small volume; rate 90."

Clinical diagnosis: Mitral disease with small heart. "Although there is no thrill and no pronounced typical presystolic murmur, the enlargement of the right heart and liver, dyspnoea, subcutaneous edema, short presystolic murmur (with heart beating 80 to 90), and accentuated second pulmonic suggest mitral 'narrowing'." Death occurred on August 26.

Postmortem Examination.—Anatomic diagnosis: sclerosis of the pulmonary artery and its branches; hypertrophy of the wall of the right ventrical; edema of the myocardium; fibrous obliteration of the pericardial sac; marked general passive hyperemia; slight ascites; edema of the loose retroperitoneal tissues, gastrohepatic ligament and wall of the gallbladder; indurative shortening of the mesentery and mesocolon (chronic passive hyperemia); moderate emaciation; slight generalized jaundice; cyanotic atrophy of the liver; atrophic emphysema of the lungs; scars of the apexes of the lungs; localized bilateral fibrous pleuritis; localized fibrous perisplenitis and perihepatitis; moderate sclerosis and fatty changes of the aorta; slight coal-pigmentation of the lungs and tracheo-

bronchial lymph glands; slight canities; cysts of the ovaries; bilateral hydrosalpinx; corset constrictions (three) of the liver; vaccination scars (three) of the right arm; tongue shaped left lobe of the liver; fetal lobation markings of the kidneys.

The body was that of a white woman, aged 40, weighing 86 pounds (39 Kg.) and by actual measurement 167 cm. long. The scalp hair was dark brown, slightly tinged with gray. The sclerae were light yellow. The superficial veins of the face and neck, lower extremities and lower part of the trunk were engorged with blood and very prominent. The body nourishment was fair. The neck was long and the front lower portion full. The junction of the neck with the shoulders was almost a right angle. Edema of the subcutaneous tissues was not observed. The breasts were small, the areolae pigmented dark brown. Body heat was present and rigor mortis had not yet developed in the extremities. The thorax was narrow from front to back.

The subcutaneous fat in the midline of the trunk in front was orange-yellow and from 5 to 7 mm. thick. There was about 205 Gm. of brown watery fluid in the peritoneal cavity. Strandlike fibrous adhesions were observed between the spleen and diaphragm. The retroperitoneal tissues were slightly fluctuant. The splenic and hepatic flexures of the colon were not pronounced, the course of the colon being semicircular. The mesocolon everywhere averaged about 10 cm. long. The diaphragm on the right side extended up to the fourth rib, on the left side to the middle of the fifth rib. The loops of the small bowel were reddish purple and collapsed. The lower margin of the liver on the right side was about 1 cm. above the costal margin. The lower margin of the left lobe was narrow and tongue shaped, and it extended 9 cm. caudad to the tip of the xiphoid process. The lower pole of the spleen was about 4 cm. above the costal margin.

The costal cartilages were soft. The lungs did not collapse when the chest was opened. Multiple firm threadlike fibrous adhesions were present between the lungs and the chest wall posteriorly at the lower lobes, and at the apex of the right lung. The maximum transverse diameter of the heart was 14.5 cm. The pericardial cavity was almost entirely obliterated by fibrous adhesions. The main branches of the pulmonary arteries were not obstructed. The blood in the right heart chambers was dark red, almost black, fluid and abundant. The blood did not clot readily when it left the vessels. The medial surface of the left lung was adherent to the pericardial sac by a few fibrous strands.

There was only adipose tissue in the thymic body. The thyroid gland was about twice the normal size, symmetrical and pale brown-purple, and in surface made by sectioning there was an abundance of colloid material and clumps of old fibrous tissue in irregular regions from 2 to 6 mm. in diameter.

In the lining of the aorta there were bright yellowish orange, irregular elevations and some that were gray, involving about one half of the thoracic portion and three fourths of the abdominal portion. Transverse superficial ridges were present in the lining of the renal arteries. The lining of the inferior vena cava, iliac or renal veins was unchanged. The loose retroperitoneal tissues were gelatinous and greenish yellow from the fluid in them.

The cortices of the suprarenal glands were mottled orange-yellow and red. The kidneys were about the normal shape. Surfaces made by sectioning were purple; the medulla was much darker than the cortex, and a moderate amount of bloody fluid appeared on the surfaces. The cortical markings were distinct. Noteworthy changes had not occurred in the renal pelves or ureters.

The lining of the esophagus was smooth and light gray purple. The tracheobronchial lymph glands were dark purple to black and formed a soft mass caudad to the bifurcation of the trachea, triangular and each side about 5 cm. long. Surfaces made by sectioning were moist and dark purple.

In the main portion of the pulmonary artery and the main branches there were bright yellowish orange plaques, involving about one third of the lining.

Stringy fibrous adhesions were seen between the diaphragmatic surface of the right lung and the diaphragm. The right lung weighed 215 Gm., the left 175 Gm.

A yellow, watery fluid was present in the fibrous adhesions in the pericardial sac at the base. The heart with the pericardial sac, but with most of the extrapericardial adipose tissue removed, weighed 330 Gm. The pulmonic ring was 8 cm. in circumference. The cusps were normally thin. The cavity of the right ventricle from the apex to the pulmonic ring was about 9 cm. long. The trabeculae carneae of the right ventricle were much larger and firmer than those of the left, and averaged from 2 to 4 mm. in diameter, whereas those in the left ventricle were slender. The wall of the pulmonary conus in front was 7 mm. thick. The front wall of the right ventricle, exclusive of the trabeculae carneae, was about 6 mm. thick; at the apex from 2.5 to 3 mm. The tricuspid ring was 13 cm. in circumference. A foramen ovale was not present. Surfaces made by sectioning the front wall of the right ventricle were composed of large regions of brown moist myocardium. In other places the myocardium was brown and dry.

Orange-yellow, irregular, soft, slightly elevated regions, similar to those in the main branches, were present in the lining of the branches of the third and fourth divisions of the pulmonary arteries. The lungs were crepitant throughout. At the apex of the left lung there was a thin scar in the pleura. The lung tissue was inelastic, but the lungs partly collapsed after they were opened. The course of some of the second and third divisions of the pulmonary artery was slightly tortuous. The circumference of the main branch to the left lung was 2.5 cm., of the first divisions 1.5 cm. The total pulmonary arterial vascular bed did not appear to be greater than usual. The pulmonary veins were unchanged.

The mitral ring was 10 cm. in circumference, the aortic 6.5. The mouths of the coronary arteries were patent. The lining of the left circumflex branch was light gray and smooth. The right coronary artery was almost twice as large as the left, its lining everywhere smooth.

The spleen weighed 255 Gm. The connective tissue of the gastrohepatic ligament was light yellowish green and markedly edematous. The biliary lymph glands were gray-yellow, and very wet, and some were about 2.5 cm. long. The lining of the portal vein was smooth and gray-white, that of the hepatic artery intact. The lining of the common, cystic and hepatic bile ducts and of the gallbladder was normally trabeculated and light brown. The gall bladder wall was from three to four times normal thickness. The lower fifth of the front of the liver was firm from gray-white stellate scars in the capsule. Surfaces made by sectioning the liver were moderately bloody, moist and mottled light brown and brown purple to almost black in the upper part of the right lobe. The lobules were coarse. There was a marked increase in fibrous tissue in the periportal spaces. The liver weighed 1,040 Gm. The scars in the capsule did not extend into the liver.

In the stomach there was about 100 cc. of light green semisolid material mixed with mucus. The lining was generally pink and normally rugate. The pancreas was light purple on surfaces formed by cutting. Its duct was normally translucent. There were a few transverse wrinkles in the lining of the splenic artery. The lining of the lower half of the rectum was light gray.

Histology.—In the microscopic preparations of the dorsal portion of the upper lobe of the right lung, stained with hematoxylin and eosin, most of the alveoli were empty. The alveolar walls were thin in a few places, but in others about normal thickness; the capillaries were filled with erythrocytes. In the arteries from 0.25 to 0.5 mm. in diameter, the intimal and subintimal coats were thickened by fibrous connective tissue so that they were from two to three times as thick as the middle muscular coat, diminishing the lumens, most of which were eccentric, to about one sixth or one seventh of the greatest diameter of the vessel. This fibrous tissue in most places was slightly vacuolated. The media in most of the arteries was about the same thickness throughout. The adventitia

Fig. 1.—The marked diminution of the lumens of the smaller pulmonary arteries, due to extensive proliferation of fibrous tissue in the intimal and subintimal layers, is characteristically illustrated. Magnification × 140.

was composed of loose fibrous tissue. The lumens of the arterioles (precapillary arterioles) were considerably more diminished than those of the larger arteries (figs. 1 and 2). Round cell infiltrations were not observed in the walls of the arteries and perivascular tissues. In a few of the arterioles, organized thrombi completely or partially filled the lumens. Moderate coal pigmentation of the peribronchial tissues was present. The lumens of most bronchi were empty, and the mucous membrane was normally thin. Some of the alveoli in the dorsalmost parts of the lung were collapsed.

In sections stained with Weigert's elastic tissue stain, the amount of elastic tissue varied considerably. In the larger branches where the lumen was eccentric

the thin portion of the intimal and subintimal layers was rich in elastic fibers, whereas in the thicker portions there were only thin strands. In the precapillary arterioles elastic tissue was sparse; in fact, there was none in many such vessels internal to the media. In the pulmonary veins important changes had not occurred.

In the dorsal and ventral portions of each lobe and the middle of each lobe, the changes were as extensive as in the right upper lobe, the only difference being that dorsally there was slight atelectasis, and in the ventral portion distention of the alveoli.

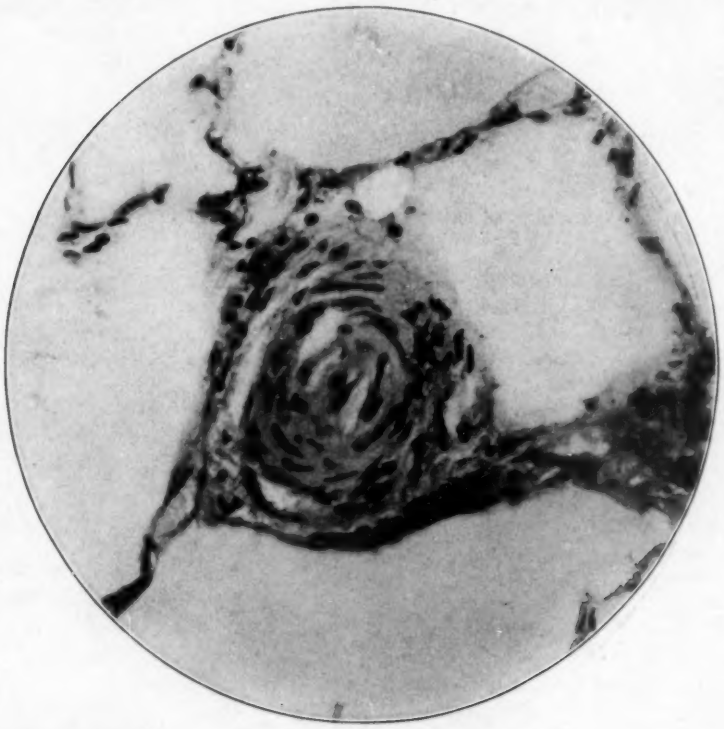

Fig. 2.—The striking microscopic alteration in primary sclerosis of the pulmonary artery and its branches is represented by the changes of this arteriole; everywhere throughout the lungs, there are arterioles with lumens correspondingly reduced, and occasionally some are found which are obliterated by thrombi. Magnification × 350.

The yellowish brown elevated regions in the intima of the pulmonary artery were like those in the main portion.

In sections of the lung and pulmonary arteries stained with sudan III, fat was found in the larger branches in the intima, but there was practically none in the precapillary arterioles.

In sections of the liver, the central portions of most lobules were made up of dilated vascular spaces and extensive destruction of hepatic cords was observed. Noteworthy changes had not occurred in the periportal spaces.

In the wall of the right ventricle at the pulmonary conus there was considerable edema of the interstitial tissues. In a few regions near places where the myocardial fibers had almost disappeared, there was a moderate infiltration of plasma cells, a few round cells and polymorphonuclear leukocytes. Striation of most of the muscle cells was indistinct. The brown pigment close to the nuclei was sparse. In the back wall of the right ventricle there were a few regions in the myocardium from one half to one third of the size of a low power field, in which the muscle bundles were thin and separated by fibrous tissue and an abundance of pink granular material. The intima of some of the arterioles was slightly thickened, in some places equaling the media, but nowhere was there diminution of the lumen similar to that in the vessels of the lungs. In this part of the heart there was an abundance of brown pigment in muscle cells near nuclei. In the adventitia of the arterioles and perivascular tissues noteworthy changes had not occurred.

In the thyroid gland most of the alveoli were filled with colloid-like material, a few of them empty and small. The epithelium of most alveoli was in a single layer, but in a few places it was from two to three layers deep.

In the suprarenal glands engorgement of the capillaries was seen, with erythrocytes and slight thickening of the walls of some of the veins, chiefly the adventitia.

In the kidneys most of the glomeruli were intact. The capsules were thin and tufts engorged with red cells. In the larger arteries at the junction of cortex and medulla the intima was slightly thickened with fibrous tissue. The intima of the larger arterioles in the cortex was not changed. About one glomerulus in fifty was completely hyalinized and shrunken. In the medulla there was marked engorgement of the veins.

SUMMARY

Clinically, the illness of this patient corresponded closely with those cases described by Posselt and Eppinger. Cyanosis was present for four years, but evidence of myocardial insufficiency did not become conspicuous until eight months before death. The cyanosis was never as severe as in Ayerza's disease. Hypertrophy of the right ventricle was demonstrated four years before death. Edema of the subcutaneous tissues appeared eight months before death, but shortness of breath was never proportionate to the edema or cyanosis. This illness, as in many of the other studies, was confused with mitral stenosis.

The lung fields during the period of maximum shortness of breath and cyanosis were clear in roentgenograms (fig. 3). The outline of the left auricle indicated that this portion of the heart was not enlarged. These observations are inconsistent with mitral stenosis or other valvular or myocardial diseases of the left side of the heart when the myocardium is obviously inadequate.

The chest was not enlarged, which helped to exclude hypertrophic emphysema of the lungs. The excursion of the lungs posteriorly was about 2 cm., and roentgenograms did not show any evidence of extensive pleural adhesions.

Development of the disease insidiously, following a severe pulmonary infection, when the patient was 32 years old, excluded congenital heart disease.

Posselt described spasmodic severe thoracic pain resembling that of angina pectoris, but usually in the right side. Four years before death, thoracic pain was present in our patient somewhat resembling the paroxysms of angina pectoris, occurring during exertion, and she "would have to stop walking." At that time a diagnosis of acute pleuritis was made.

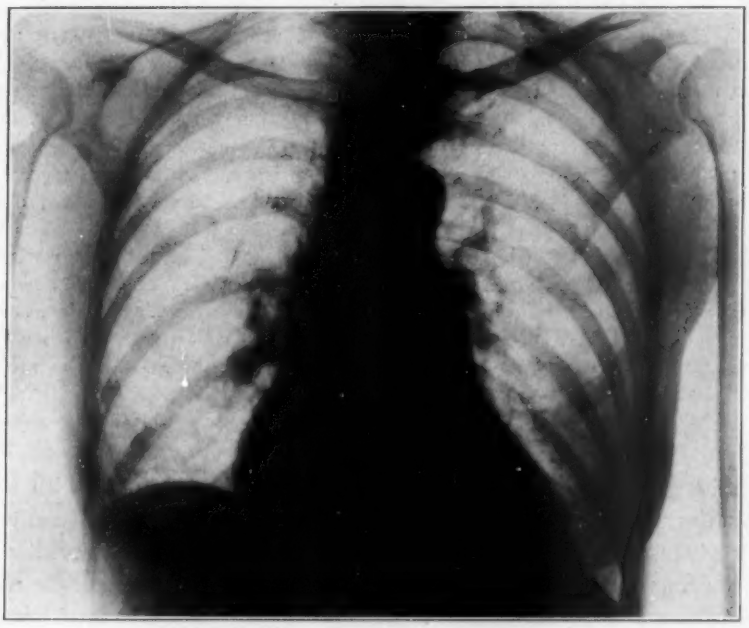

Fig. 3.—Roentgenogram made nine days before death; at this time cyanosis, subcutaneous edema and shortness of breath were pronounced; enlargement of the heart to the right, clear lung fields and bowing in the upper half of the pulmonary and left auricular areas are the outstanding characteristics.

Polycythemia is an unimportant clinical feature of the condition described by the Germans. Two blood counts, in 1922 and 1925, respectively, demonstrated a secondary anemia and leukopenia. During the terminal period the red blood cells numbered 6,080,000, the hemoglobin content was 85 per cent (Dare) and the white blood cells numbered 7,000.

Summary of Morbid Alterations.—The marked diminution of the channels of the pulmonary arterioles (figs. 1 and 2), present in all parts of both lungs, was due to intimal and subintimal proliferation of fibrous tissue in which there were retrogressive changes, without cellular exu-

date, resembling, therefore, senile arteriosclerosis. Similar alterations were present in the bronchial arterioles, but to only a slight degree. The long continued lessened flow of blood through the lungs had resulted in atrophy of the walls and diminution in the cavities of the left auricle and ventricle; in the latter the trabeculae carneae were small.

The caliber, walls and mouths of the pulmonary veins had not changed anywhere. Some authors have described stenosis of the pulmonary veins as the alteration which causes hypertrophy of the right ventricle and sclerosis of the pulmonary artery. By others it is believed that the diminution of the circumference of the larger pulmonary veins is due to atrophy of disuse.

The only thoracic deformity was a slight scoliosis, the deviation from the midline to either side being only a few centimeters.

The fibrous adhesions in the pleural cavities were less extensive than those commonly found in bodies in which cardiac alterations are not observed. It is estimated that only one fifth of the pleural cavities was obliterated by fibrous adhesions.

Hypertrophic emphysema, or genuine emphysema of Kaufmann, is the only form of pulmonary emphysema that is a primary cause for hypertrophy of the right ventricle. Compensatory and senile emphysema are associated with a large right heart only when other conditions, such as bronchiectasis and bronchial asthma, are present. In medical literature, the term emphysema of the lungs is used frequently without the type being qualified. It is well known to pathologic anatomists that hypertrophic emphysema is an anatomic entity and the one form of emphysema that is characteristically associated with hypertrophy of the right ventricle and, during life, with cyanosis and cardiac insufficiency. The lungs in our case were still somewhat elastic, collapsing considerably after removal from the body. Coal pigmentation was marked in all parts, another indication that most of the alveolar walls were still intact. The lungs were practically bloodless and the right weighed 215 Gm., the left 175 Gm., which is additional evidence against hypertrophic emphysema, in which disease the lungs usually weigh from 800 to 1,000 Gm., each. Posselt and Eppinger called attention to the paleness and bloodlessness of the lungs in primary sclerosis of the pulmonary artery, which were two characteristics of the lungs of this body.

The wall of the right ventricle was hypertrophied, especially the pulmonary conus and the trabeculae carenae. The circumference of the pulmonary ring and artery was not increased. The circumference of the main portion of the right coronary artery was twice as great as that of the left. The scars of the myocardium of the right ventricle were most numerous in the front wall. Some resembled healed Aschoff bodies.

The changes in the aorta and its main branches were not more than are frequently found in early adult life. Sclerosis was present in the small arteries of the kidneys, myocardium, spleen and other organs, but only in a slight degree.

The spleen is enlarged in Ayerza's disease. The spleen in this patient was never palpated during life, and the slight increase in weight (spleen 225 Gm.) is explained by passive hyperemia.

A large part of the pericardial sac was obliterated by fibrous adhesions, but the sac was not adherent to the chest wall or to the lungs, except by a few fibrous adhesions. We do not believe that this alteration accounts for much of the cardiac enlargement, because when enlargement of the heart is due to obliteration of the pericardial sac the left ventricle is preponderately enlarged, and the degree of change present in our case is frequently found at autopsies when there is not any demonstrable cardiac enlargement.[15]

Etiology.—A specific etiologic factor was not demonstrated by our examination. Gross or microscopic changes characteristic of syphilis were not found, and unfortunately a Wassermann test was not performed during life.

The patient suffered from two severe infectious diseases, rheumatic fever at 8 years and influenza at 32. The obliterative pericarditis and fibrous myocarditis may be attributed to the former. The patient stated emphatically that the last illness came on insidiously after influenza and pneumonia. This association is important because Le Count [16] demonstrated that one of the characteristic anatomic changes of influenza during the epidemic of 1917-1919, was necrosis of the pulmonary capillaries. Others [17] have emphasized the relation of arteriosclerosis to infectious diseases.

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15. Fatty changes and sclerosis of the pulmonary artery are frequently found at necropsies. They are most extensive when there is obstruction to the pulmonary circulation. This form of sclerosis is named secondary sclerosis of the pulmonary artery by Posselt. Following the increased number of reports of the two conditions described here, cases were reported of chronic pulmonary and cardiac diseases associated with sclerosis of the pulmonary artery (presumably secondary to obstruction of the pulmonary circulation), and the sclerosis was made the cause for many of the cardiac symptoms during life. The German authors have, therefore, emphasized the importance of excluding from the group of "primary sclerosis of the pulmonary artery," all cases in which pulmonary, cardiac or thoracic diseases are present which may obstruct the pulmonary circulation.

16. Le Count, E. R.: Disseminated Necrosis of the Pulmonary Capillaries in Influenzal Pneumonia, J. A. M. A. **72**:1519-1520 (May 24) 1919; Pathologic Anatomy of Influenzal Bronchopneumonia, ibid. **72**:650-652 (March 1) 1919.

17. Posselt (footnote 3). Jores, L.: Arterien, Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1924, vol. 2.

CONCLUSIONS

The clinical and anatomic characteristics of primary sclerosis of the pulmonary artery are described, and a report is made of one case that the authors believe is typical of this disease.

Even though primary sclerosis of the pulmonary arteries is a rare disease, its anatomic and clinical manifestations are so characteristic that it should be recognized during life, if it is borne in mind when search is being made for the cause of enlargement of the right side of the heart.

Ayerza's disease has not been defined clinically and anatomically as characteristically as primary sclerosis of the pulmonary arteries. Some of the cases reported as Ayerza's disease resemble the latter disease, but others are obscured by extensive alterations in the lungs and by associated cardiac disease.

FOLLICULAR LYMPHADENOPATHY WITH SPLENOMEGALY

A NEWLY RECOGNIZED DISEASE OF THE LYMPHATIC SYSTEM *

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The occurrence of enlargement of the lymph nodes attended by splenomegaly suggests several clinical possibilities: among them, Hodgkin's granuloma, chronic lymphatic leukemia, Cohnheim's pseudoleukemia and lymphosarcoma—all of them fatal diseases. To be added to this number is a disease which only recently has been described under the title of follicular lymphadenopathy with splenomegaly. It presents essentially the same clinical features as those conditions just enumerated, but differs in the important respect that, even if allowed to take its course over an indefinite period, it does not of necessity interfere with the patient's comfort nor threaten his safety, and when submitted to roentgen-ray therapy is susceptible of great improvement or even cure.

Clinical recognition of the disease is to be predicated only on the basis of excision and microscopic examination of an involved lymph node, the histologic changes in which are characterized by a striking degree of hyperplasia of the germinal follicles, the microscopic architecture thus differing from that of all the several conditions with which it is otherwise likely to be confounded. That the disease does not belong among the leukemias is shown by the blood picture and by histologic differences in the lymph nodes. That it does not belong among the neoplasms of the lymphoid apparatus is likewise obvious from the histology, which corresponds exactly with that familiarly encountered as a reaction in the germinal centers of localized groups of lymph nodes in association with many inflammatory or toxic conditions. Clinically, the resemblance to Hodgkin's disease is striking, but between the two confusion is impossible histologically, since the respective pictures are entirely at variance. While the nature of the provocative agent is unknown, it may be said with an approach to certainty that syphilis does not enter into the process, since in five of the six cases thus far observed the Wassermann reaction was negative and there was no reason to suspect syphilis as a result of physical, historical or microscopic evidence. In spite of this, however, because of the ubiquity of syphilis and its many and fantastic methods of display, its activity in this instance cannot be denied.

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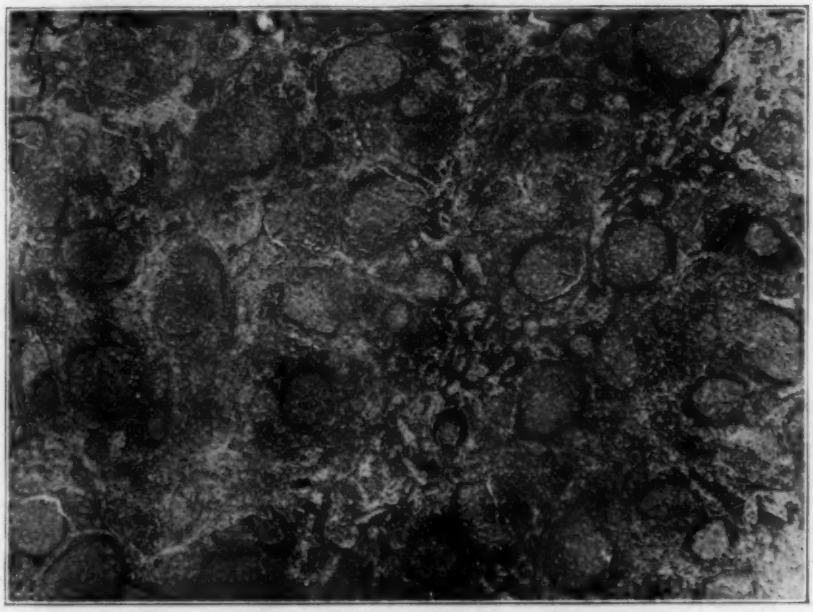
* From the Pathological Laboratories, Bellevue Hospital.

Apparently, the first case reported was recorded by Becker,[1] who, however, did not accord it the dignity of an individual position in the scale of disease. The patient was a woman, aged 33, whose illness commenced with swelling of the lymph nodes of the neck, followed in the course of the next three years by enlargement of all the superficial lymph nodes, some of which reached the size of a walnut. The spleen was massively enlarged. A lymph node removed three years after the onset of the disease was examined microscopically and found to present histologic signs of "simple hyperplasia."



Low power photomicrograph showing extensive numerical and dimensional hyperplasia of the germinal follicles in follicular lymphadenopathy with splenomegaly.

In 1925, Brill, Baehr and Rosenthal,[2] under the title of "Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen," described two cases almost identical with that previously recorded by Becker. The first case was that of a woman, aged 28, who was admitted to the hospital complaining of difficulty in breathing, and later of cough, who presented marked generalized enlargement of the lymph nodes, the

1. Becker, E.: Deutsche. med. Wchnschr. **27**:726, 1901.

2. Brill, N. E.; Baehr, G., and Rosenthal, N.: Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen, J. A. M. A. **84**:668 (Feb. 28) 1925.

individual nodes varying in size from that of a pea to that of a walnut, movable and free from tenderness. The roentgen ray showed moderate enlargement of the peribronchial nodes, particularly on the left side, thus accounting, perhaps, for the patient's respiratory disturbances. The spleen was huge, reaching from the level of the eighth rib to the anterior-superior iliac spine, and to the right for a distance of 5 cm. beyond the midline; it was smooth and not tender. Microscopic examination by Mandlebaum of excised lymph nodes from the neck and axilla "failed to show any evidence of Hodgkin's disease, lymphosarcoma or tuberculosis." On the contrary, the changes were confined to excessive enlargement of the germinal follicles. Under roentgen-ray therapy, both the splenic and the lymph node enlargements disappeared completely. The second case was that of a woman, aged 32, who complained of gradual enlargement of the abdomen of two months' duration. Both the spleen and liver were greatly enlarged, the former extending from the eighth interspace above to the brim of the pelvis below and to within 2 cm. of the midline. The cervical, axillary, epitrochlear and inguinal nodes were moderately enlarged. Because of increase in weakness, progressive anemia and evidences of blood destruction due, apparently, to disease of the spleen, splenectomy was performed. Microscopic examination of the spleen and of an enlarged lymph node removed from the abdomen showed enormous hyperplasia of the germinal follicles in both. Three months after splenectomy, the lymphadenopathy disappeared and the blood picture returned to the normal. Later, the nodes in both axillae again became enlarged, but vanished under roentgen-ray therapy.

REPORT OF CASES

CASE 1.—Several weeks ago, I received from Major Callender of the Army Medical Museum, on behalf of the registry of the American Association of Pathologists and Bacteriologists, a number of histologic preparations made from an excised inguinal lymph node, with a request for an expression of opinion as to the nature of the changes present. The node was taken from a man, aged 32, with moderate but generalized lymphadenopathy which, at the time of removal of the inguinal node, had been present for a period of five years. The individual nodes were discrete and free from pain or tenderness. Microscopic examination showed nothing noteworthy beyond excessive hyperplasia of the germinal follicles. At the time that the inguinal node was removed, the patient said that he had been aware of marked enlargement of the spleen for over a period of one year. Roentgen-ray therapy was followed by marked diminution in the size of both the lymph nodes and the spleen. Ten years have now elapsed since the commencement of the disease and the patient says that he has never suffered any inconvenience as a result of the malady, nor has he found it necessary to lose a single day from his duties.

CASE 2.—A few days after this case came to my attention, I was asked to see a patient in consultation—a girl, aged 7, who had been admitted to Bellevue Hospital because of swollen lymph nodes that had been present for a period of two and one-half years in various parts of the body. History referable to

previous abnormalities of the lymphoid system could not be obtained from the mother, except for the statement that three years before admission the tonsils had been "lanced" but "filled up again." At the time of admission, the suboccipital, cervical, axillary, inguinal and femoral nodes were moderately but distinctly enlarged. The nodes varied in size from 1 to 3 cm. and were firm, discrete and unattended by discoloration or other changes in the overlying skin, or by local heat or tenderness. The tonsils were greatly increased in size. The spleen was palpable two thirds of the distance from the xiphoid to the umbilicus; it likewise felt firm and smooth and was not tender. Shortly after admission, an enlarged lymph node was removed from the inguinal region and, on microscopic examination, I did not find any histologic indications of disease other than marked hyperplasia of the germinal follicles, the cellular unit in the hyperplastic areas consisting of a cell somewhat larger than the ordinary lymphocyte and with a less richly chromatic nucleus—corresponding, in other words, to the lymphoblast normally encountered in the germinal centers. Since lymphoid hyperplasia in the inguinal nodes occurs in a variety of conditions, I requested that a node be removed from the child's neck. This was done, and microscopic examination revealed alterations identical with those encountered in the node from the inguinal region.

CASE 3.—Still another case recently came under my observation. A Spaniard, aged 33, a laborer, was admitted to the surgical service of Dr. C. J. MacGuire, at St. Vincent's Hospital, complaining of "stomach trouble" and mild jaundice, among other things, both of about six months' duration. Physical examination revealed a moderate degree of generalized jaundice, together with numbers of enlarged lymph nodes in both axillae, more marked on the right side, and palpable lymph nodes in both inguinal regions. The nodes were discrete and freely movable, painless and all of about the same size, measuring approximately 1 to 1.5 cm. in diameter. The spleen was felt 6 cm. below the costal margin on the left side and the liver was palpable at the level of the umbilicus. The blood count showed a secondary anemia and the Wassermann reaction was negative. Roentgen-ray examination of the chest failed to reveal any indications of enlarged lymph nodes. Because of the nature of the symptoms referable to the region of the stomach, Dr. MacGuire thought it advisable to perform an abdominal exploration. On doing so, he found an immense growth of lymph nodes in the retroperitoneal region, extending entirely across the abdomen, as far upward as the region of the pancreas and as low as the brim of the pelvis. The lymph nodes were closely packed and varied in size from 1 to 6 cm. At the time of operation, numerous enlarged lymph nodes were observed in the immediate vicinity of the common bile duct; compression by these nodes was thought to give rise to obstructive changes in the biliary drainage system and, hence, to the jaundice of which the patient complained.

An enlarged lymph node, removed from the abdomen for microscopic examination, measured 5 by 3 by 1 cm. and presented, on section, a perfectly smooth, homogeneous, cream colored substance. Histologic examination revealed an extraordinary degree of hyperplasia of the germinal follicles, both numerical and dimensional, and moderate streaklike interfollicular fibrosis. The follicles were rounded, sharply circumscribed, with variable numbers of small, deeply staining lymphocytes at the extreme periphery, and composed of cells somewhat larger than the ordinary lymphocyte, with a pale, poorly chromatic nucleus—in other words, lymphoblasts. Mitotic figures were fairly numerous, and among the lymphoblasts was a sprinkling of small cells with richly chromatic

pyknotic nuclei, representing, apparently, lymphoblasts in the process of disintegration. In places, also among the lymphoblasts, larger mononuclear cells were found, in the cytoplasm of which an occasional phagocytized pyknotic body was seen.

COMMENT

Localized lymph node and splenic lymphadenosis are recognized conditions, but the occurrence of a disease characterized by widespread or generalized enlargement of the lymph nodes, superficial, deep or both, attended by splenomegaly and characterized histologically by changes marked almost exclusively by numerical and dimensional hyperplasia of the germinal follicles, adds a new note to the pathology of the lymphoid system and commands consideration from the aspect of diagnosis, since the disease in question, unlike those with which it is likely to be confounded clinically, is benign from the standpoint of prognosis, and promising from that of treatment.

EOSINOPHILIA IN THE VERMIFORM APPENDIX*

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The local eosinophilia in normal and pathologic appendixes is obvious. The present study was undertaken to determine, if possible, criteria whereby the degree or location of eosinophilia in appendical tissues might serve in establishing the type of lesion. References to eosinophilia in the appendix are rare in the literature and the few textbook statements on this topic are sometimes misleading.[1]

It was deemed essential to establish a normal criterion before attempting a grouping of pathologic cases. Material for this purpose was fixed in 5 per cent formalin immediately after removal at operation, or within one or two hours after death in necropsy specimens. The importance of early fixation becomes evident after little experience in this work as eosinophils rapidly lose their staining affinities and disintegrate after tissue death. Fixation in alcohol should be avoided. Few if any eosinophils stain after alcohol fixation, an observation attested by several investigators. Tissue was embedded in paraffin in the usual manner, or else frozen sections were made after formalin fixation. Delafield's hematoxlyn was used as a nuclear stain. In the majority of instances alcoholic eosin was used to identify acidophil granules; in some cases, following the nuclear staining, the sections were placed in weak aqueous eosin for twenty-four hours. Preparations should be stained in either solution of eosin in such a manner that confusion may not arise between the appearance of eosinophil and other granules. Care should be taken to avoid overstaining. The appendixes of three fetuses of four months did not show eosinophils in any layer. Sections from the distal, middle and proximal third were examined. A six and a seven months fetus showed eosinophils in the mucosa averaging one per high power field ($\times$ 440). Morbid changes were not noted in any of these fetuses. An average of two eosinophils per field was found in the appendix of a new-born infant who died of intracranial hemorrhage several hours after birth and had never received nourishment by mouth. A new-born child who had received milk by mouth and lived two days presented an average of four eosinophils per field. The appendix of a nine months old infant who died of crushing injuries showed an average of six eosinophils per field.

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* From the Pathological Laboratory of the Bushwick Hospital.

1. Delafield and Prudden: A Textbook of Pathology, ed. 11, New York, William Wood & Co., 1919, p. 781.

Nielsen [2] has made a study of local eosinophilia in the appendixes of fetuses and new-born children. He comes to the conclusion that eosinophils appear in the appendix at the fifth month of fetal life, coincident with, or shortly after, the appearance of eosinophils in the peripheral blood stream. The number of cells increases in direct proportion to increase in size and weight of the organism. Fetuses and infants with syphilis show considerably greater numbers of eosinophils per field than normal persons of corresponding ages. New-born infants who have taken nourishment by mouth show a greater number of eosinophils per field than new-born babes who have not had any nourishment. Heidenhain and others have shown that eosinophils disappear from the intestinal tract of dogs after a seven day fast and reappear after feeding. The passage of food through the intestinal tract increases local eosinophilia in the appendix.

The occurrence of tissue eosinophilia in the appendixes of normal fetuses, new-born babes and infants has been described by Aschoff,[3] Schmidt,[4] Stutz [5] and Schwarz.[6] The number and location of these cells varies with the age of the person. The majority of the cells are found in the mucosa; rarely are eosinophils found in the other layers of the appendix normally. The numbers increase during childhood, and eosinophils are found in increasing numbers about the borders of the lymph follicles. Larger numbers appear directly beneath the epithelial cells and range themselves in crescents about the bases of crypts. Appendixes of normal structure in apparently normal persons always show some degree of eosinophilia. This observation has been made for adults of both sexes by Aschoff, Howard and Perkins,[7] and Warren and Forman.[8] The latter present a detailed study of sixty normal organs all of which showed a moderate local eosinophilia.

Combining the gross and microscopic data in 150 cases in which the appendix was not involved clinically, thirty-nine were chosen as normal

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2. Nielsen, M.: Vom Vorkommen eosinophiler Zellen im Appendix des Foetus und des neugeborenen Kindes, Acta gynec. Scandinav. **2**:370, 1923.

3. Aschoff, L.: Die Wurmfortsatzentzündung, Jena, 1908.

4. Schmidt, J. E.: Beiträge zur normalen und pathologischen Histologie einiger Zellarten der Schleimhaut des menschlichen Darmkanales, Arch. f. mikr. Anat. **66**:12, 1905.

5. Stutz, E.: Ueber eosinophile Zellen in der Darmschleimhaut des Darmkanals, Inaugural Dissertation, Bonn, 1895.

6. Schwarz, E.: Die Lehre von der allgemeinen und örtlichen Eosinophilie, Ergebn. d. allg. Pathol. u. path. Anat. **17**:137, 1914.

7. Howard, W. T., and Perkins, R. G.: Observations on the Origin and Occurrence of Cells with Eosinophile Granulations in Normal and Pathological Tissues, Johns Hopkins Hosp. Rep. **10**:249, 1902.

8. Warren, J. H., and Forman, J.: Observations of the Occurrence of Eosinophilic Leucocytes and the Granule Cells of Paneth in the Vermiform Appendix, Anat. Record **12**:455, 1917.

morphologically. Every one of the organs showed eosinophilia, the number of eosinophils per field varying from five to sixteen. The majority of the cells was located in the mucosa, just below the epithelium, frequently clustered about crypts. Smaller numbers are seen at the periphery of the lymph follicles. A few occurred in the subserous connective tissue. It is rare to find one in the muscularis. Eosinophils are never observed within lymph follicles in normal appendixes. A similar observation has been recorded by Warren and Forman. The eosinophils in question are identical with the eosinophils of the blood and bone marrow. They have bilobed nuclei, as a rule, and stain intensely with the oxidase stain of Winkler, as applied by Warren and Forman. I have been unsuccessful in staining material with Goodpasture's oxidase stain. Occasionally, eosinophils identical with those seen in adjacent tissues were found in small blood vessels. Migration through the vessel wall was not seen. In rare instances, eosinophils were found passing through the epithelium. The majority of such cells showed evidences of cytoplasmic and nuclear degeneration. Eosinophils in the content of the lumen were not seen. Transitions from plasma cell to eosinophil as noted by Howard and Perkins have not been observed. The evidence is in favor of the view that the eosinophils seen in appendical tissues are of myeloid origin. Indications of local genesis of eosinophils were not evident in the material studied.

Since eosinophils appear at an early period of fetal life in the appendical mucosa, a small number are therefore normal. The sudden increase with the intake of food is also coincident with the entrance in the intestinal tract of fecal bacteria. Fifteen sections stained by the Gram-Weigert method [9] failed to show any phagocytosis of bacteria by eosinophils. The fact that eosinophils respond to the stimulus of foreign proteins entering the tissues or blood stream suggested the possibility of appendical eosinophilia being evidence of reaction to bacterial or other foreign protein passing through the mucosa of the appendix. The stagnation of fecal material within the appendical lumen would favor such bacterial invasion. Nielsen states that an increased local eosinophilia has been observed especially in the appendical mucosa on which intestinal parasites have been resting. In this series of normal appendixes the segment of appendix chosen for examination, the presence or absence of feces from the lumen and the presence or absence of macroscopic food particles seemed to be without influence on the number and distribution of eosinophils in the mucosa. A specimen from a person claiming to be a vegetarian for eight years prior to removal of the appendix showed the usual mucosal eosinophilia. Factors such as age,

9. Mallory and Wright: Pathological Technique, ed. 7, Philadelphia, W. B. Saunders Company, 1921, p. 250.

sex, weight, diet and constipation failed to account for increase or decrease of appendical eosinophilia. The conclusion may be drawn that the normal appendixes of infants, children, adults and the aged of both sexes show a tissue eosinophilia limited almost entirely to the mucosa.

A hard and fast rule in regard to the degree of eosinophilia in various pathologic conditions could not be established, yet the number and location of the eosinophils was an aid in diagnosis in many instances. Especially is this true in mild acute appendicitis and in chronic appendicitis. Inflammatory lesions as studied in 400 cases always showed increases in the number of eosinophils. Of further import is the finding of eosinophils within lymph follicles and in the muscularis and serosa.

Numbers ranging from twenty-one to fifty-four eosinophils per field were noted in acute appendicitis of mild and moderate degree. One specimen of severe acute appendicitis showed the enormous number of 126 eosinophils per field. This increase was limited largely to the subepithelial connective tissue and perilymphoid tissue. Eosinophils penetrating the mucosa were frequently seen. In almost every section eosinophils were found within the lymphoid follicles, a condition never encountered in normal organs. Eosinophils appear in the tissues affected by the early congestion and edema of inflammation, the numbers increasing until the point of suppuration is reached. With acute interstitial and diffuse inflammations all layers are infiltrated with eosinophils. They appear in the submucosa, between the muscle fibers and in the congested and edematous subserous connective tissue. A certain percentage of the cells show degenerative cytoplasmic and nuclear processes. Where foci of suppuration or necrosis have begun, the eosinophils are found in decreasing numbers. An area of inflamed tissue shows a high eosinophil count whereas an area of suppuration or necrosis shows a relatively low eosinophil count with a high percentage of these cells degenerating. It is rare to see eosinophils in the exudate in the lumen. With suppuration the pus in the lumen has never been observed to contain eosinophils. With suppuration the eosinophils disappear, being replaced by the neutrophilic polymorphonuclear cells.

The marked muscosal infiltration and perilymphoid distribution of eosinophils may be brought out strikingly by means of Winkler's oxidase stain. The eosinophils stand out as intense, blue-black staining corpuscles. This reaction indicates that the infiltrating cells are of myeloid origin. That eosinophils may respond as phagocytic cells is known. Downey [10] quotes an interesting case in which the cells of a pleural exudate were very active as phagocytes. He refers to other cases men-

10. Downey, Hal: Reactions of Blood and Tissue Cells to Acid Dyes under Experimental Conditions, Anat. Record **12**:429, 1917.

tioned in the literature. Ringoen [11] and others have observed the phagocytosis of erythrocytes and hemoglobin by eosinophils. Ten sections from acute suppurative inflammatory lesions of the appendix stained by the Gram-Weigert method failed to show phagocytosis of bacteria by eosinophils. In a case of ruptured ectopic pregnancy in which there had been free blood in the peritoneal cavity for forty-eight hours, the subserous connective tissue beneath the swollen serosal cells showed an average of twenty-five eosinophils per field. Staining by Okijama's method [12] showed a positive reaction in all eosinophils. This stain is said to be elective for hemoglobin. Warren and Forman cast some doubt on this statement, claiming that the stain will react positively with eosinophil granules. The evidence for phagocytosis of hemoglobin in this case is therefore doubtful. In an appendix removed from a patient with tuberculous peritonitis, tuberculous periappendicitis was present without any evident lesion of the other layers. The eosinophils in the greatly thickened serous coat averaged twenty-nine per field. In four cases of pelvic suppuration in which periappendicitis was secondary, considerable numbers of eosinophils were found in the subserous connective tissue. One section showed a dilated venule with five eosinophils in the lumen. Migration through the wall was not observed. This process has not been observed in a single instance in this series of cases.

In mucosal lesions resulting in ulceration, the ulcer base does not show any eosinophils. Occasional eosinophils are seen at the borders of the ulcer. In the majority of cases, one does not need the evidence of eosinophilia to make a diagnosis of acute appendicitis. Yet in mild acute cases, the increase of eosinophils and their occurrence within the lymph follicles is a distinct aid. The observation of eosinophils in acute inflammation of the appendix has been discussed by Kühnel,[13] Howard and Perkins, Weir,[14] Aschoff, Loele,[15] Oehler [16] and Schwarz.

Chronic inflammatory disease also leads to increased local eosinophilia in the appendix. The degree is, as a rule, distinctly less than in acute inflammation. It is limited largely to the mucosa, except in chronic periappendicitis. Chronic irritants, such as intestinal parasites, may

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11. Ringoen, A. R.: On the Origin of Eosinophil Leucocytes of Mammals, Anat. Record **18**:255, 1920-1921.

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cause eosinophil reaction especially beneath the mucosa directly in contact with the irritant, it is said. Two appendixes from children, both containing oxyurides, showed normal numbers of eosinophils. Eosinophils are prominent cellular elements in the chronic appendicitis which follows the subsidence of an acute or subacute attack of appendicitis. The study of appendixes removed at "interval" operations reveals this clearly. The cells are found in profusion in the mucosa, lymphoid follicles and submucosa. Especially large numbers are seen about the bases of crypts and about lymph follicles. Occasionally, recent muscularis scars show moderate numbers of eosinophils. With the production of fibrous tissue, the numbers of eosinophils decrease. Chronic obliterating appendicitis presents few or no eosinophils, depending on the amount of lumen remaining. With the disappearance of the lumen, mucosa and lymphoid tissue the eosinophils are characteristically absent. Kühnel has drawn attention to this fact. Fibrous scars of the muscularis, which in some instances are the sole evidence of previous acute attacks, are not characteristically free of eosinophils. Chronic inflammatory disease with eosinophils also presents considerable numbers of plasma cells.

Two cases of carcinoid of the appendix, of the type suggesting a basal cell epithelioma, with islands of epthelial cells, showed an average of eight eosinophils per field in sections in which lumen was not present. The eosinophils were arranged primarily about the islands of epithelial cells. Such eosinophil reaction has been noted in the inflammatory processes developing about neoplastic tissue.[6] In such cases, suppuration leads to the disappearance of eosinophils.

The eosinophils seen in all types of appendical disease are identical in morphology with eosinophils of the blood and bone marrow. Their staining reactions also resemble those of the myeloid eosinophils. Rarely, mononuclear eosinophils are seen which resemble eosinophilic myelocytes. This has been interpreted as an evidence of local eosinophil development. It would seem more logical to assume a myeloid origin of these cells. Attempts at correlating tissue eosinophilia with blood eosinophilia fail in cases of acute or chronic appendicitis. In all likelihood, if a transient vascular eosinophilia does occur in acute appendicitis, the majority of cases are encountered far too late in the course of the disease to detect it. The average hospital patient is rarely seen before the disease is well advanced.

The evidence of this study and of others points to the myeloid origin of the eosinophils in normal and pathologic appendixes. The burden of proof rests on those who claim that local proliferation of eosinophils occurs. In areas showing numerous eosinophils, the forms seen in bone marrow which present unusual staining reactions of the granules were not observed. That the function of the eosinophil in the appendix is phagocytic is more than likely, but direct evidence is lacking.

CONCLUSIONS

Eosinophils are normal cellular elements in the appendix from the fifth month of fetal life to old age. Eosinophils normally occur in the mucosa in small numbers. They are seen occasionally in the serosa, and rarely in the muscularis. They are never observed within lymph follicles in the normal appendix.

In acute inflammatory lesions, eosinophils occur in increasing numbers, and then disappear with the advent of suppuration and necrosis. Periappendicitis calls forth a local eosinophilia in the serosa. With obliteration of the lumen, eosinophils disappear from the appendical tissues.

The eosinophils of normal and pathologic appendixes are probably of myeloid origin. Evidence of local proliferation is not obtained in normal or pathologic organs.

936 Bushwick Avenue.

Laboratory and Technical Notes

A CONVENIENT APPARATUS FOR BLOOD COUNTING

E. R. Serles, Brookings, S. D.
Dean of Pharmacy, South Dakota State College

Under the old method of filling the blood pipets, many difficulties are encountered. The novice finds it difficult to watch the tiny column of blood rise to 0.5 and at the same time to hold the rubber tube so that kinks do not appear which will cause trouble when he places his tongue on the opening in the mouth piece. In order to eliminate this difficulty I used a 2 cc., hypodermic syringe and shortened the rubber tube to about 1 inch (2.5 cm.). This worked much better, but the flexibility of the rubber tube still caused slight changes in the length of the air column above the blood and gave rise to errors when the pipet was carried from the blood droplet to the diluting fluid. The new apparatus, shown in the figure which consists of an ordinary hemacytometer pipet with the top end reinforced and ground to fit the nozzle end of a 2 cc. Luer syringe, answers the purpose well.

In order to insure perfect connection, the nozzle of the syringe barrel *A* may be coated with a film of castor oil. This not only insures a close fit of

Pipet and syringe for blood counting.

the two parts, but it also allows for the easy removal of the syringe when one wishes to transfer it to other pipets. A drop of oil on the plunger of the syringe facilitates its operation.

The advantages of this apparatus are as follows:

The operator may take up the blood column with one hand, since a slight raising of the plunger by the thumb and forefinger is sufficient to fill the pipet to 0.5. The other hand is free to use as occasion demands. The eye may be placed on a level with the graduations on the pipet. The column remains fixed unless the plunger is moved, and if the plunger is covered with castor oil, accidents rarely occur. As soon as sufficient diluting fluid has been drawn into the bulb of the pipet, the apparatus may be rested in the hollow between the thumb and forefinger of the left hand and rotated with the right, as one rolls a pencil between the thumb and fingers. The syringe attachment facilitates the washing of the pipets. One syringe may be used for as many pipets as desired. However, using one for red and one for white cells is more convenient.

I use another simple device which was designed by Dr. R. C. Sherwood, consisting of a rubber stamp which is a replica of one sixteenth of the counting field of the slide. This enables the examiner to record his count systematically.[1]

1. The pipets were ground by the Central Scientific Company, Chicago, Illinois. The rubber stamp was manufactured at the Northwestern Stamp Works, St. Paul, Minn.

Notes and News

Philadelphia Pathological Society Elects.—The Philadelphia Pathological Society has reelected Eugene Opie, president; J. Harold Austin, vice-president; Baldwin Lucke, secretary; Morton McCutcheon, recorder.

Death of Edwin Garvey Kirk.—Dr. Edwin Garvey Kirk, aged 46, head of the department of pathology and surgical pathology at the Chicago Post-Graduate Medical School, died recently.

Centenary of Société Anatomique.—This society, founded in 1826 by Cruveilhier, recently celebrated its hundredth anniversary by discussing the pathologic anatomy of pulmonary tuberculosis.

Dedication of Simpson Institute for Medical Research at Ann Arbor.—The institute stands in front of the University Hospital, which supplies its nursing and janitor services. Research will be directed primarily toward problems connected with pernicious anemia. Cyrus C. Sturgis is the director, and Raphael Isaacs, assistant director.

Harmsworth Fund for the Study of Ulcerative Endocarditis.—The committees in charge of this fund invite the active cooperation of clinical and laboratory workers throughout the world. "It is proposed to make grants to individual workers, whether in Great Britain or in any other part of the world whatsoever, on account of their contributions to chemical and laboratory research. This would include subsidies to workers, whose present efforts lie in the direction likely to yield results of importance in the problem under consideration; and also to other workers to whom special and new lines of research will be suggested; also grants to those who contribute statistics, data, results of private experiment, research or observation. The powers possessed by the Trustees enable them to disburse moneys by way of bonus to any worker whose contribution is judged to be of exceptional or indeed of any value. These powers include the option to close the Fund altogether by making a grant of the whole of the Capital remaining at any time to a worker whose contribution shall be judged by the Committee of Trustees, acting with the Scientific Committee, to have finally disposed of the present obscurity overlying the knowledge of the disease and thus to give the medical profession 'control' over the disease." The secretary of the fund is Dr. P. Seymour Price, 41, Sloane Gardens, London, S. W. I., England, who will welcome communications from interested persons.

University News, Promotions, Resignations and Appointments.—Kano Ikedo has assumed the directorship of the laboratories of St. Luke's Hospital, St. Paul.

Frederick H. Dieterich, formerly professor of pathology at the Medical College of South Carolina, has been appointed director of the laboratories of the Good Samaritan Hospital in Cincinnati.

J. P. Lovely has been appointed fellow in pathology at the Mayo Foundation, Rochester, Minn.

C. M. Medlar, associate professor of pathology in the medical school of the University of Wisconsin and associate pathologist at the Wisconsin General Hospital, has resigned and will leave at the end of the present academic year to take a position with the Mt. McGregor Sanitarium of the Metropolitan Life Insurance Company in New York.

Walter Simpson has accepted the position of pathologist to the Miami Valley Hospital at Dayton, Ohio. The hospital has 425 beds.

The University of Maryland has been granted increased appropriations by the legislature for extensive improvements in and additions to buildings occupied by its schools of medicine, dentistry and pharmacy. This reconstruction will result in improved laboratory facilities for pathology and bacteriology.

Earl B. McKinley has resigned as associate professor of bacteriology in the College of Physicians and Surgeons of Columbia University, New York, to accept appointment as field director in the International Health Division of the Rockefeller Foundation with assignment to the Bureau of Science, Manila, P. I.

Wellcome Bureau of Scientific Research, London, Reopened.—The Wellcome Bureau of Scientific Research in London, founded in 1913 by H. L. Wellcome, has been reopened after reconstruction and enlargement of the buildings. C. M. Wenyon, the protozoologist, is director-in-chief. A main purpose appears to be to encourage and support research by volunteer workers who are free to follow their own line and to publish their results as they see fit. The Wellcome Museum of Medical Science has been given additional space.

Approved Clinical Laboratories.—A revised list has been published (*J. A. M. A.* **88:**838, 1927) of the clinical laboratories outside of hospitals that have been approved by the Council on Medical Education and Hospitals of the American Medical Association. There are now 145 laboratories on this approved list. The standard of measurement is the "Essentials of an Approved Clinical Laboratory," which has been prepared with the cooperation of pathologists and other experts in laboratory work. The Council is prepared to maintain the investigations necessary to determine the worthiness of clinical laboratories for inclusion in its approved list.

Meeting of Die Deutsche Vereinigung für Mikrobiologie.—Die Deutsche Vereinigung für Mikrobiologie will meet in Vienna in the week beginning June 5, 1927. The two principal subjects for discussion are experimental cancer research and active immunization against bacteria.

Abstracts from Current Literature

Pathologic Physiology

Intraperitoneal Transfusion of Citrated Blood (in Rabbits). J. Martin Sansby, Am. J. Dis. Child. **30**:659, 1925.

An intraperitoneally produced plethora of citrated blood has an inhibitory effect on the hemopoietic function of the bone marrow, similar in nature to that produced by the intravenous route. This substantiates further the viability of the red blood cells introduced by intraperitoneal transfusion.

Spermatogenesis after Injection of Testis Material. W. J. Quick, Am. J. Physiol. **77**:51, 1926.

Following from one to five subcutaneous or intraperitoneal injections of homologous spermatozoa or macerated testis material in white rats, no apparent specific effect on testicular activity was observed. Both motile spermatozoa and successful matings were obtained with these animals, tests being made from three days to four months after the last injection.

In some cases the injected material passing down from the peritoneal cavity through the open inguinal ring caused the formation of cysts which from their size or location caused mechanical displacement of the testis. Where this resulted in removal of the testis from its scrotal location, degenerative changes were observed, and the writer emphasizes the importance of the normal scrotal environment of the testis.

H. E. Eggers.

The Activity of Displaced Testes and Its Bearing on the Problem of the Function of the Scrotum. C. R. Moore, Am. J. Physiol. **77**:59, 1926.

On the removal of the testes of the rat and guinea-pig from their scrotal location to one in the subcutaneous tissue, it was found that spermatogenetic function continued from three to nine months, but spermatozoa were not formed during this period. In the case of removal of one testis to a subcutaneous location, and of the other to an intra-abdominal site, the latter did not carry on spermatogenetic activity. In one case, such an intra-abdominal testis redescended into the opposite scrotal sac, after an indeterminate stay in the abdomen; this testis was found to be entirely normal ninety-six days after the transplantation.

The writer concludes that the functional interference of transplantation is due to difference of environment alone, presumably temperature variation serving as the determining factor, and he considers the principal function of the scrotum as that of a heat-regulatory device.

H. E. Eggers.

Cryptorchid Testes and Testicular Hormone Production. R. M. Oslund, Am. J. Physiol. **77**:76, 1926.

In a study of natural cryptorchid testes of man, dog, sheep and pig, the cells of the semeniferous tubules were found to be active, and to produce other cells, which in some cases resembled primitive spermatogonia. Spermatogonia developed from these in the cryptorchid testis show spermatogenic activity

after placement in the scrotum. It follows that not only are germ cells present in cryptorchid testes, but also that these cells actually undergo a certain degree of division.

As to hormone production, the writer concludes that it takes place in the absence of mature spermatogonia, spermatocytes, spermatids and spermatozoa, but from the material it could not be determined whether the germinal epithelium or the interstitial cells were concerned in its production. H. E. Eggers.

Ligation of Vasa Efferentia in Rats. R. M. Oslund, Am. J. Physiol. **77**:83, 1926.

The retention of spermatogenic products in the testis of the rat, following ligation of the vasa efferentia, results in an increase in size and a hardening of the testis. This reaches its height in forty-eight hours and within seven days there is a diminution in size and hardness. This is caused by a decrease in, if not a cessation of, spermatogenesis, and by the absorption of the now necrotic retained material. Progressive degeneration occurs during the course of the experiment, that of the germinal epithelium being accompanied by a decrease in size of the semeniferous tubules. In part this is compensated for by an increase of intertubular space, in part it causes atrophy of the organ as a whole. Hypertrophy of interstitial cells was not observed. H. E. Eggers.

The Effect of Variations in Protein Intake on the Acidity of the Secretion of the Fasting Stomach. F. Hoelzel, Am. J. Physiol. **77**:166, 1926.

Of principal interest was the finding, in a human subject, that excessive protein in the diet caused a decrease in the acidity of the secretion of the fasting stomach. A wide range of proteins proved effective in this connection. From this, and from the fact that functional rest, either by fasting or by protein restriction, was followed by an increased acid secretion, it is suggested that the phenomonon is one of secretory fatigue, and that this fatigue may play a part in the natural regulation of protein intake in food. H. E. Eggers.

The Basal Metabolism of a Normal Young Man as Affected by a Tropical Residence of One Year. W. D. Fleming, Am. J. Trop. Med. **5**:283, 1925.

A normal white man, aged 22, was used in the tests. Basal metabolic rates, respiratory quotients, etc., were taken seven months after arrival in the tropics and again after a thirteen months' interval. In the first series of tests the basal metabolic rate average 3 per cent. minus; for the second series it averaged 7 per cent. minus. E. M. Hall.

A Study of Fasting Blood Sugar and Urea in Non-Diabetic Patients. H. J. John, Ann. Clin. Med. **5**:340, 1926.

John analyzed the fasting blood sugar and blood urea content in 1,000 non-diabetic patients. The blood sugar content is quite uniform in all decades, in the majority of cases lying betwen 80 and 110 mg. per hundred cubic centimeters. A slight but uniform ascent occurs with each succeeding decade. Blood urea retention is higher in the later decades of life. The rise of the blood sugar is low compared with the markedly increased urea. This suggests that the same underlying factor does not govern both of these elements. Urea is a metabolite and blood sugar is not a metabolite; the kidneys govern the first and affect the second but slightly. Walter M. Simpson.

THE POSSIBLE RELATIONSHIP BETWEEN ACROMEGALY AND DIABETES. H. J. JOHN, Arch. Int. Med. **37**:489, 1926.

In general, hypopituitarism is accompanied by an increased carbohydrate tolerance and hyperpituitarism by decreased tolerance, but this is not an absolute rule. In most reported cases and in the two here reported, the onset of acromegaly preceded the onset of diabetes by many years. Patients in whom diabetes is associated with acromegaly, if not controlled, are as subject to acidosis and coma as those with the ordinary cases. Hypersecretion of the posterior part of the pituitary gland seems to produce hyperglycemia and glycosuria. Whether this is the predisposing factor is not certainly established; the incidence of diabetes in acromegaly is rather high, but, whatever the primary factor, the metabolic disturbance is due to a decreased insulogenic secretion. It may be that the factor that produces hyperpituitarism may also have some influence in producing the decreased insulogenic function which brings about diabetes. Diabetes is always due to the same immediate factor, namely, a diminution of the insulogenic function, and whether it is or is not associated with pituitary dysfunction, its course does not vary and the same treatment is indicated as in the ordinary case.

S. A. LEVINSON.

THE MECHANISM OF INSULIN ACTION. E. F. MUELLER, H. J. WIENER and R. v. E. WIENER, Arch. Int. Med. **37**:512, 1926.

A deposit of insulin in the body acts by a nerve stimulation which increases the glycogen forming function of the liver. This nerve stimulation is conducted parasympathetically. The effect is active as long as the insulin deposit exists as such. It is particularly strong if the insulin deposit is made in the skin because of its close relationship to the autonomic nervous system. The nerve effect is weaker after deposition of the insulin in organs in which absorption takes place rapidly, for instance, the subdermal tissues, and is lacking after intravenous administration. The hormone effect in the circulation and in the body tissues is relative to the dose but the neural effect of insulin does not depend on the dosage. Simultaneously with the beginning of the absorption from the insulin deposit and with the consequent entrance of insulin into the circulation the direct hormone effect is manifested. The nerve effect decreases simultaneously with the diminution of the insulin deposit outside of the circulation, and disappears as the last part of the insulin deposit is absorbed.

S. A. LEVINSON.

THE THERAPEUTIC USE OF DIETS LOW IN WATER AND IN MINERAL CONTENT. N. M. KEITH, F. H. SMITH and MARY WHELAN, Arch. Int. Med. **37**:550, 1926.

Carefully controlled diets of low mineral and water content are both practicable and effective in the treatment of cases of edema and ascites. The diets may be varied in protein and caloric value with little increase in mineral or water content. There have been no demonstrable ill effects from the continued use of these diets.

S. A. LEVINSON.

WATER METABOLISM. II. FUTHER OBSERVATIONS. EDMUND ANDREWS, Arch. Int. Med. **37**:559, 1926.

The amount of "free" water in the tissues varies with the alkalinity of the blood as measured by the carbon dioxide combining power of the plasma. The

exact mathematic accuracy of this proportion, when hypertonic salt solution is used as the dehydrating agent, is evidence that the elimination of water in these experiments is purely a physicochemical phenomenon and that no "vital" factors need be considered.

S. A. Levinson.

Pressure on the Ventral Nervous System in Its Relation to Hyperglycemia: Chronic Piqure. W. Z. Tychowski and Caroline Crowell, Arch. Int. Med. **37**:567, 1926.

This work was calculated to reproduce pathologic conditions taking place in cases of disease of the nervous system associated with hyperglycemia, in which either local mechanical compression of the medulla oblongata or general rise of the cerebrospinal fluid tension, followed by compression of the whole central nervous system is essential. The analogy consisted in applying local mechanical pressure on the medulla oblongata and general hydrostatic pressure on the whole central nervous system. Both procedures, applied experimentally on cats, were followed by a rise in the sugar content of the blood. Hyperglycemia, thus artificially produced in animals, represents in pertinent clinical cases a chronic type of piqure, which may have several factors concerned in its causation.

S. A. Levinson.

Diseases of the Liver: V. A Comparative Study of Tests for Hepatic Function in Certain Diseases of the Hematopoietic System. C. H. Greene and H. M. Conner, Arch. Int. Med. **38**:167, 1926.

Greene and Conner have shown that serum albumin is of value in differential diagnosis between hemolytic anemias and the ordinary secondary types. The "indirect" diazoreaction when associated with an increase in serum bilirubin is characteristic of an icterus of hemolytic origin and is of diagnostic value. The "direct" diazoreaction in hemolytic jaundice is associated with gallstones.

S. A. Levinson.

Chemical Changes in the Blood During Fasting in the Human Subject. W. J. Lennox, Marie O'Connor and Margaret Bellinger, Arch. Int. Med. **38**:553, 1926.

Observations of chemical changes in the blood made during and subsequent to thirty fasting periods of epileptic and normal subjects showed the following: During fast nonprotein and urea nitrogen varied considerably from day to day, with a tendency toward increased concentration; amino-acid nitrogen remained remarkably constant and uric acid rose independently of other constituents examined. In the period of refeeding nonprotein and urea nitrogen and uric acid fell to subnormal levels. Sugar fell to a low level during the first week, rising again as the fast progressed. Concentration in plasma was constantly lower than in whole blood. Inorganic phosphorus and calcium remained constant, and cholesterol and fibrin showed both increase and decrease. Plasma bicarbonate was greatly reduced, coincident with increase in total acid excretion. In a three day fast without water, there was evidence of unusual increase in protein metabolism.

S. A. Levinson.

The Regulation of the Flow of Bile and Pancreatic Juice Into the Duodenum. G. H. Copher and S. Kodama, Arch. Int. Med. **38**:647, 1926.

Tonus and peristalsis in the duodenum are of great importance in the regulation of the flow of bile into the duodenum. This control is independent of

factors other than pressure of the bile in the common duct. The duodenal wall exerts a like control over the discharge of pancreatic juice from the pancreatic duct. Food, drugs and chemicals that affect tonus and peristalsis are factors in the regulation of the flow of bile and pancreatic juice into the duodenum.

S. A. Levinson.

The Blood Sugar Curve in Mental Disease: II. The Schizophrenic (Dementia Precox) Groups. J. Kasanin, Arch. Neurol. & Psychiat. **16**:414, 1926.

In the blood sugar curves of forty patients of the author and those of 154 patients with schizophrenia reported in the literature, a characteristic blood sugar curve was not found.

Roy Grinker.

Sodium Chloride Metabolism in Cutaneous Burns and Its Possible Significance for a Rational Therapy. E. C. Davidson, Arch. Surg. **13**:262, 1926.

In thirty-one patients presenting cutaneous burns of varying degree and extent a decided fall in the sodium chloride of the whole blood and the plasma was found. This could not be explained by the presence of fever fluid loss, blood concentration or disturbance of the renal threshold, but appeared to be due to a disturbance of the chloride metabolism with retention in the tissues. In view of this the authors suggest the administration of sodium chloride to correct the deficiency.

N. Enzer.

Vital Capacity of Negro Race. W. G. Smilie and D. L. Augustine, J. A. M. A. **87**:2055, 1926.

The vital capacity of the negro race, in both sexes and for all age groups studied, is markedly lower than the vital capacity of the white race. When calculated from surface area, the difference is from 15 to 20 per cent in children, and from 25 to 35 per cent in adults.

The growth curves of weight and of standing height of white and negro children correspond closely, but negroes have a shorter trunk length than whites. When vital capacity is calculated from stem length, therefore, there is less discrepancy between the vital capacity of the two races than when it is calculated from surface area or standing height, the results being only 10 to 15 per cent lower than in the whites.

Authors' Summary.

Hypophysectomy and Replacement Therapy in Relation to Basal Metabolism and Specific Dynamic Action in the Rat. G. L. Foster and P. E. Smith, J. A. M. A. **87**:2151, 1926.

The basal metabolism of totally hypophysectomized rats was found to be about 35 per cent below the average of our series of normal animals. The metabolic rate of these animals may be restored to normal by daily anterior pituitary homotransplants or by daily injections of thyroid extract, but not by daily injections of posterior lobe extract.

The specific dynamic action of glycocoll is absent in hypophysectomized animals and apparently can be restored only by replacement of both anterior and posterior lobe, but not by either one alone.

Authors' Summary.

EXPERIMENTAL HIGH JEJUNOSTOMY IN THE DOG, WITH BLOOD CHEMICAL STUDIES. RUSSELL L. HADEN and THOMAS G. ORR, J. Exper. Med. **55**:795, 1926.

Dogs with simple high drainage of the jejunum lived from two to five days. This is a shorter average length of life than that which occurred with simple obstruction at the same location. The chemical changes of the blood were similar to those occurring in high intestinal obstruction. They differed, however, from pyloric and duodenal obstruction in that the carbon dioxide combining power did not show any constant change and the chlorides did not show such a marked fall. Animals with simple jejunostomy and closure of tube to prevent drainage proved that the operation done was not the cause of death in these cases. Ileostomy twelve inches above the cecum did not produce the profound disturbance of high jejunostomy. It is probable that some dogs would live indefinitely with low drainage of the ileum.

Treatment with sodium chloride solution definitely prolongs the life of dogs with high jejunostomy. The cause of the rapid death in high jejunostomy apparently differs from that in high intestinal obstruction. Sodium chloride solution will not protect in this condition to as great an extent as in high intestinal obstruction. Whether death is caused by dehydration, toxemia, loss of chlorides or loss of other important elements is not known. Fasting is not to be considered because of the short duration of life.

AUTHORS' SUMMARY.

A REVIEW OF RECENT ADVANCES IN THE STUDY OF BLOOD SUGAR AND DIABETES. ARTHUR DIGHTON STAMMERS, Physiol. Rev. **6**:630, 1926.

For the most part this review is not adapted for summarizing, since each section really represents a summary in itself of the work published on the particular subject during the past two years. However, a brief indication of the scope of each section, together with any outstanding points, is now given.

1. The nature of the blood sugar, despite a considerable amount of fresh evidence, remains undetermined.

2. The distribution of sugar between corpuscles and plasma is still doubtful, but it seems, from the evidence available, that the greater part at least of the sugar is found in the plasma.

3. The concentration of sugar in arterial blood is usually slightly greater than that in venous blood and, ordinarily, differences do not exist in this respect between venous and capillary blood.

4. The number and variety of physiologic conditions which influence glycemia are considerable, and individual variations also exert an effect in this connection.

5. The effect of different drugs, internal secretions and inorganic salts has been the subject of attention and the work published in detailed.

6. Variations in the blood sugar content have been noticed in diseases other than diabetes.

7. The factors which are responsible for the glycolysis which takes place when blood is allowed to stand are still obscure. Bacterial action is partly but not entirely concerned in this. The rate and degree of disappearance of the sugar are inconstant and it is probable that a variety of factors take part in bringing about this condition. By bacterial action, oxidation to saccharic and mucic acids appears to take place, but if the action of bacteria is inhibited by toluol, the reducing power of the blood still disappears, although in this case the glycolysis seems to take a different path, since neither saccharic nor

mucic acid appear to be formed under these circumstances. It is suggested by some observers that glycolysis is less in diabetic than in normal blood. This, however, seems to be denied by the majority of opinions and the author's experience in this connection points to there not being any significant differences between the two types of blood. Some work in connection with the effect of different anticoagulants is reported, but this is not at present sufficient for the formation of a definite opinion. The sugar content of protein-free filtrates does not appear to remain constant, in the author's experience, although it has been demonstrated to be so by another worker. A possible explanation for this discrepancy in results is offered.

8. Dextrose tolerance tests are valuable in the diagnosis and treatment of diabetes and as these are simple to carry out and as they convey information which could not be obtained in any other way, their employment should become a matter of routine practice.

9. Various points in connection with the preparation of insulin are detailed. Most of these are directed toward the attainment of a more efficient and cheaper product. The chemical properties, so far as they have been worked out, are detailed. It has not, so far, been possible to determine the constitution of insulin.

10. Insulin may be obtained from a variety of sources, both animal and vegetable. The yield from fish is stated to be ten times as great as that from mammalian pancreas.

11. The work done on the physiologic effects of insulin is voluminous, and ninety-nine authorities are quoted in this section alone, which is divided up by thirteen subtitles. These deal with the effects of insulin in relation to glycemia, blood cells, blood pressure and blood volume, cerebrospinal fluid, phosphorus, lipoids, the liver, the pancreatic islet tissue, the nervous system, epinephrine, respiratory exchange and metabolism, heat production, thyroid secretion and certain miscellaneous reactions.

12. The secretion of insulin and its action are modified by a variety of external factors among which may be mentioned drugs, including anesthetics, inorganic salts and the nervous system. The importance of allowing for individual variations in animals in interpreting results is emphasized.

13. Certain points dealing with the physiologic assay of insulin are reviewed.

14. Mention is made of the more important features of insulin therapy, in the light of experience gained during the period of its practice.

15. Brief indications are given of recent developments in methods for blood sugar estimation. Where the apparatus and solutions are available several reliable methods exist, and of these, it is probable that Maclean's is the most popular. They are all laboratory methods, however, and attention is drawn to one devised by the author (p. 899 of this number of the ARCHIVES, which is considerably simpler than any hitherto described and which it is hoped may be useful as a substitute where the carrying out of other methods is impracticable.

AUTHOR'S SUMMARY.

THE EXCRETION OF WATER, UREA AND CHLORIDES IN EXPERIMENTAL OXALATE NEPHRITIS. J. SHAW DUNN and NORA A. JONES, J. Path. & Bacteriol. **28**:483, 1925.

Rabbits were given from 40 to 75 mg. of sodium oxalate intravenously, the larger doses being given in 50 mg. and 25 mg. doses about forty minutes

apart. When urea retention had been established in the tubular nephritis due to oxalates, a copious excretion of urea and a lowering of the retention could be brought about by inducing water diuresis; chloride was excreted with the excess of water. The view that urea, like chloride, is excreted in the glomerular filtrate, is in agreement with these results. The theory is advanced that the urea retention in this type of experimental nephritis is explained by the inability of the damaged tubule cells to prevent indiscriminate reabsorption of glomerular filtrate containing urea from the tubules into the tissues of the kidney.

E. M. HALL.

THE LOCUS OF BILE PIGMENT FORMATION. E. MELCHIOR, F. ROSENTHAL and H. LICHT, Klin. Wchnschr. **5**: 37, 1926.

Extirpation of the liver prevents the development of toluylene diamine and phenylhydrazine icterus. It is concluded that the liver is the chief site of bile pigment formation.

ARTHUR LOCKE.

CHOLESTERIN METABOLISM AND HAIR GROWTH. R. JAFFÉ, Klin. Wchnschr. **5**:507, 1926.

The rate of hair growth may be dependent on the rate of cholesterol metabolism. The external application of salves containing cholesterol may produce an accelerated and uniform regrowth of hair over depilated areas of rabbit skin.

ARTHUR LOCKE.

INSULIN RESISTANT DIABETES. E. FRANK, Klin. Wchnschr. **5**:688, 1926.

An especial type of neurorenal, insulin-refractory diabetes is reported.

ARTHUR LOCKE.

THE MINIMAL PROTEIN CONSUMPTION IN ACROMEGALY. E. KRAUSS, Klin. Wchnschr. **5**: 700, 1926.

The increases observed in acromegaly in the minimal amount of protein consumption and in the amount of uric acid excreted cannot be regarded as characeristic indications of an altered functioning of the hypophysis.

ARTHUR LOCKE.

THE PATHOLOGIC METABOLISM OF GOUT. K. HARPUDER and L. SPITZ, Klin Wchnschr. **5**: 706, 1926.

It is unlikely that there is any simple cause for the pathogenesis of gout The deposition of urates in a tissue is probably only the consequence of a predisposing physicochemical abnormality.

ARTHUR LOCKE.

THE VARIABILITY OF HORMONE ACTION. H. ZONDER and H. UCKE, Klin. Wchnschr. **5**:1861, 1926.

The ability of insulin to reduce the blood sugar when injected into rabbits is not changed by the passage through it of a 110 volt electric current of 30 milliampere strength for twelve hours, nor by dialization for several days. After electrodialysis its effect on the blood sugar is entirely lost. This indicates an internal rearrangement of the insulin molecule from an active to an

inactive form. The variability of the colloid character of tissue cells has, therefore, an analogy in the structural and biologic modifiability of the hormones.

J. D. WILLEMS.

STOMACH AND KIDNEY AS EXCRETORY COMPETITORS. W. LIPSCHITZ, Klin. Wchnschr. **5**:2008, 1926.

After preparing the stomach by ligation of the pylorus and thorough lavage, dextrose, sodium salicylate and sodium iodide are injected intravenously. The gastric juice, the blood and the urine are then quantitatively analyzed for these substances and the relative amounts compared. Dextrose appears in the stomach when its concentration in the blood is sufficiently high. The excretory threshold of the stomach for dextrose is considerably higher than that of the kidney. The dextrose excretion of the stomach equals from 1 to 20 per cent of that of the kidney. Salicylic acid does not appear in the stomach. Iodine is excreted by the stomach until the iodine-chlorine proportion in the gastric juice is equal to that in the blood. The amount of iodine excreted by the stomach varies from 6 to 600 per cent of that excreted by the kidney. Iodine in small doses is, therefore, suitable for a functional test of the stomach.

J. D. WILLEMS.

THE PRODUCTION OF UTERINE HYPERTROPHY BY THE SERUM OF PREGNANT WOMEN. F. G. TRIVIÑO, Klin. Wchnschr. **5**:2022, 1926.

Subcutaneous injection of the serum of pregnant women causes a marked hypertrophy of the uterus in immature rats. The substances which produce this are diffusible, alcohol soluble and thermostable. In their production not only the ovaries, but also the uterus and the placenta take part.

J. D. WILLEMS.

THE MECHANISM OF EGG TRANSPORT IN THE FALLOPIAN TUBES OF THE RABBIT. A. WESTMANN, München. med. Wchnschr. **73**:1793, 1926.

The abdomen is opened, the intestines are pushed up and a large loop of cecum is permanently stitched into place in such a way that an unobstructed peritoneum-lined space is made for the uterus and adnexae. A celluloid window is affixed to the ventral body wall. This allows observation of the uterus, ovaries and fallopian tubes at any desired time.

As an egg follicle matures the tube undergoes marked rhythmic dilatations and muscular contractions and peristaltic movements. At the time of ovulation the lateral ligament contracts, bringing the fimbriated end of the tube into close contact with the ovary. Thus, the ovum is sucked directly into the fallopian tube and transported to the uterus by active movements. A ripening follicle always stimulates the tubal contractions; a corpus luteum arrests them. In castrated animals the tubal action is constant but weak.

J. D. WILLEMS.

CENTRALLY CONDITIONED INHIBITION OF COLONIC PERISTALSIS. W. FELTKAMP, Deutsche Ztschr. f. Nervenh. **93**:259, 1926.

The author describes four cases of paralytic ileus, in three of which operation was performed for organic obstruction. In all but one case obstipation persisted and at death megacolon was found. In each case a lesion was found

between cord segments A_{12} and L_2 which the author considers furnished a continuous irritation to the cells of origin of the hypogastric nerve, resulting in an overbalance of its function and stasis of the bowel.

ROY GRINKER.

SUGAR METABOLISM IN CHRONIC EPIDEMIC ENCEPHALITIS AND PARALYSIS AGITANS. R. A. TKATSCHEW and W. W. AXENOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:391, 1926.

In chronic epidemic encephalitis and in paralysis agitans a disturbance in sugar metabolism was found, in that an induced alimentary hyperglycemia showed a delay in the return to normal. This was attributed to an involvement of the central regulating mechanisms in the diencephalon.

ROY GRINKER.

PHAGOCYTOSIS AND MOVEMENT OF EPITHELIUM OF URINARY BLADDER, GALLBLADDER AND TONGUE OF THE FROG IN VITRO. SHIN-ICHI ISHIKAWA and SHIRO SHINMOMURA, Acta derm. **6**:475, 1925.

Small pieces of the epithelium from the urinary bladder and gallbladder of the frog were cultivated in autoplasma at room temperature. The epithelium of the urinary bladder showed active movement in the form of membraneous expansion and ameboid movement at the advancing border, marked after twenty hours. The epithelial cells showed phagocytic activity, engulfing granules of China ink. The epithelium of the tongue and gallbladder behaved similarly, although that of the gallbladder was much less active.

B. R. LOVETT.

THE INFLUENCE OF CERTAIN POISONS ON THE FUNCTION OF THE ISOLATED SUPRARENAL GLAND. A. J. KOUSNETZOW, Arch. d. sc. biol. **25**:291, 1925.

The author studied the effect of strychnine, curare, picrotoxin, veratrine, morphine, cocaine, quinine, and mercuric chloride. The strength of the action was determined by the colorimetric reaction of Folin and the reaction of the vessels of the isolated rabbit's ear. The reaction on the suprarenal vessels was studied at the same time. Strychnine produced the strongest exciting effect, veratrine and picrotoxin a weaker effect. Curare, mercuric chloride, and cocaine augmented or decreased the secretion according to the dose. Quinine 1:1,000 lessened the secretion. Morphine produced only a slight effect.

CONTRIBUTIONS TO THE INFORMATION CONCERNING LIVER FUNCTION TESTS. PART 3. ON THE COLOR DIAGNOSTIC SIGNS FOR THE LIVER. TORU OKA, Tohoku J. Exper. Med. **7**: 94, 1926.

Determinations of the relative amounts of dyes in the bile and urine of dogs after intravenous injections of 0.1 cc. of 5 per cent solutions were made with twenty-nine dyes. Correlation of these results with studies of certain physicochemical properties (acid-alkaline reaction, kataphoresis, Tyndall's phenomenon and collodion membrane permeability) of the dyes indicates that those in high grade colloidal states and those in semicolloidal solutions (nearly true solutions) whose membrane permeability is impaired by being mixed with serum both eliminated through the liver, while the semicolloids which do not lose membrane permeability when mixed with serum are excreted through the kidneys.

ETHEL B. PERRY.

ABILITY OF TISSUE CELLS TO ABSORB AND FIX SUGAR AND ITS RELATION TO THE ACTION OF INSULIN AND TO DIABETES. TOSHIO KUROKAWA, Tohoku J. Exper. Med. **8**:54, 1926.

The absorption of sugar by the body cells goes on undisturbed in the diabetic patient as in the normal person. The absorbed sugar is fixed only by normal metabolic assimilation, which fails in the diabetic patient, so the sugar circulates and passes into the urine. Insulin does not influence absorption but restores the lost power of fixation. The polyuria associated with the glycosuria is due to the water secretion which is provoked by the excreted sugar.

FROM AUTHOR'S SUMMARY.

SOME INFLUENCES OF PANCREATIC HORMONE UPON THE LYMPH. SHIGEHIRO KATSURA and KISHIRO KOZUKA, Tohoku J. Exper. Med. **8**:91, 1926.

Following the injection of pancreatic hormone, the thoracic lymph of dogs is changed so as to cause hyperglycemia when it, in turn, is injected into rabbits. Normal lymph causes hypoglycemia. Exclusion of this lymph from the body, however, suppresses either partly or completely, the convulsions that follow the injection of the hormone. Hypoglycemia, therefore, is not the sole direct cause of the convulsions. The sugar content of the thoracic lymph falls after the injection, but remains slightly higher than that of the carotid serum. The fats and lipoids in the thoracic lymph increase about four or five hours after the injection of pancreatic hormone; after injections of epinephrine hydrochloride they decrease; and in starved normal animals the content fluctuates. An increase in the lipoid content is accompanied by a fall of blood sugar and a decrease by an elevation of the blood sugar. The nitrogen content does not change conspicuously.

FROM AUTHORS' SUMMARY.

Pathologic Anatomy

ENDOMETRIOSIS OF THE SAC OF A LIGHT INGUINAL HERNIA, ASSOCIATED WITH PELVIC PERITONEAL ENDOMETRIOSIS AND ENDOMETRIAL CYST OF THE OVARY. J. A. SAMPSON, Am. J. Obst. & Gynec. **12**:459, 1926.

Sampson describes a case of endometriosis associated with a left ovarian endometrial cyst and an inguinal hernia on the right side which contained endometrial tissue. Pigmented scars were seen in the anterior and posterior culdesac. These scars contained newly formed connective tissue and phagocytes. One of the scars in the anterior culdesac contained endometrial tissue. The theories concerning the possible origin of such misplaced endometrial tissue are fully discussed. Since the tubes were patent, Sampson believes the endometrial tissue originated from a back flow of menstrual blood. This acts as an irritant, and bits of endometrial tissue if present can more readily implant themselves. The pigmented scars without associated endometriosis had their source in menstrual blood not containing any endometrial tissue. Endometrial implantation takes place the same way as implantation of cancer fragments, the menstrual blood in this case settling in the dependent portion of the pelvic peritoneum and in the inguinal hernia.

A. J. KOBAK.

THE SIGNIFICANCE OF UTERINE MUCOSA IN THE FALLOPIAN TUBE, WITH A DISCUSSION OF THE ORIGIN OF ABERRANT ENDOMETRIUM. E. NOVAK, Am. J. Obst. & Gynec. **12**:484, 1926.

In seven fallopian tubes Novak found endometrial tissue, not in the menstrual phase, lying free in the lumen; these particles of tissue were too large to have

passed through the intestitial portion of the tube and must have entered through the fimbriated end. In two of the seven cases endometrial tissue was found in the ovary. Novak has failed to see any menstrual regurgitation in thirteen patients operated on during menstruation. That endometrial tissue can undergo retrograde transportation also seems unlikely, since the tubal peristalsis and ciliary action is toward the uterine cavity. Menstrual endometrum, even if it could, in exceptional cases, undergo retrograde transportation, would have little chance of implanting itself because of the poor viability of the tissue and of the length of its time in transit. Novak offers the suggestion that the organs affected by endometriosis have a common embryologic source, namely the celomic epithelium of the urogenital folds, which retains certain developmental potentialities under abnormal conditions. Possibly the ovarian secretion may play some part in the later development. Novak, therefore, does not accept Sampson's view of the implantation of regurgitated menstrual endometrium as a frequent cause of endometriosis, and believes that Jacobson has shown only that living, virile endometrium is capable of transplantation.

A. J. Kobak.

The Relief of Experimental Arterial Anoxemia by Compressed Air. C. Ferdinand Nelson and Parke Woodard, J. Path. & Bacteriol. **28**:507, 1925.

Normal rabbits were anesthetized and placed in a compressed air chamber in which the pressures varied from 1059 to 1065 mm. of mercury above that of the atmosphere. An average increase in arterial oxygen saturation of 4.2 per cent. resulted and an increase in carbon dioxide content of 6 per cent. Compressed air was found to relieve anoxemia in the rabbit, produced by pleurocentesis. Compressed air also completely relieves anoxemia produced by injecting a 20 per cent. solution of gum arabic into the trachea of the rabbit. The use of compressed air as a therapeutic agent is discussed.

E. M. Hall.

A Study of Hyperplasia of the Bone Marrow in Man. Francis W. Peabody, Am. J. Path. **2**:487, 1926.

Careful microscopic study was made of the femoral marrow from a typhus patient because in it the stages from atrophic to hyperplastic marrow could be followed easily. The first change is the appearance of venous sinusoids, establishment of circulation in intersinusoidal capillaries and proliferation of capillary endothelium. Later precursors of red cells appear in capillaries and the picture suggests their origin from capillary endothelium. The first islands of marrow cells consist of megaloblasts attached to endothelial cells or free in capillary spaces.

Fibril Formation by Human Lutein Cells. Ward H. Cook, Am. J. Path. **2**:503, 1926.

Hitherto undescribed fibrils have been demonstrated in the marginal cytoplasm of fully developed human lutein cells. The fibrils tend to form a network enclosing each cell. The term xanthoglia is proposed to designate these fibrils.

AMYLOIDOSIS OF THE ADRENALS AS A CAUSE OF ADDISON'S DISEASE. W. C. HUNTER and H. P. RUSH, Ann. Clin. Med. **5**:404, 1926.

Amyloidosis of the suprarenals of sufficient degree to produce Addison's syndrome is rare. To six cases from the literature, Hunter and Rush add one in which the signs of Addison's disease developed in a person known to have advanced pulmonary tuberculosis and marked renal insufficiency. At necropsy, the anticipated tuberculosis of the suprarenals and kidneys was not found, but in its stead, advanced amyloidosis, involving chiefly the zona fasciculata and zona reticulosa of the suprarenal cortex and the glomeruli of the kidneys.

WALTER M. SIMPSON.

CHOLESTEATOMATOUS CYSTS. REPORT OF CASE INVOLVING THE MAXILLA. J. M. T. FINNEY and E. HANRAHAN, Ann. Surg. **84**:295, 1926.

A woman, aged 64, presented a large bony-walled cyst in the maxilla lined by thin squamous epithelium which contained atrophic dermal glands. The cyst was filled with brownish-red cholesteatomatous material. Ten years previously, all of the patient's teeth had been extracted because of pyorrhea alveolaris.

N. ENZER.

CHRONIC AND ACUTE ARTERITIS OF THE PULMONARY ARTERY AND OF THE PATENT DUCTUS ARTERIOSUS. KARL SCHLAEPFER, Arch. Int. Med. **37**:473, 1926.

Chronic and acute arteritis of the pulmonary artery and of the patent ductus arteriosus has been observed in nineteen cases. To two of these cases in which no additional valvular lesions were found, a third is added. In all nineteen cases, the picture was that of a subacute bacterial endocarditis with the signs of a patent ductus arteriosus. The seat of the arteritis is undetermined. Satisfactory evidence is not at hand to determine the influence of the force of the blood flow passing from the aorta through the duct into the pulmonary artery. The anterior wall of the pulmonary artery and the pulmonary orifice of the duct are the places of predilection. Dilatation of the stem of the pulmonary artery is often accompanied with a patent ductus arteriosus; in cases of arteritis, an aneurysmal bulging results at the site of the thrombus on the vessel wall. Narrowing (coarctation) of the descending aorta is an anomaly frequently associated with patent ductus arteriosus. It facilitates the blood flow through the duct and thereby increases the traumatism to a circumscribed part ofthe anterior wall of the pulmonary artery.

S. A. LEVINSON.

GASTRIC AND DUODENAL ULCER. A. WINKELSTEIN, Arch. Int. Med. **37**:541, 1926.

Superficial ulcers or erosions of the stomach or duodenum occur owing to various local and general causes, but heal perfectly in most persons. In certain subjects the lesion progresses and takes on the features of chronicity. This is the characteristic of ulcer as a disease entity. The usual explanations, mostly referable to local conditions, for the failure to heal seem incomplete. It is suggested that some general bodily condition, interfering with the physiology of healing, may be present. An excessive response to stimuli on the part of the nerves and tissues, locally or generally may furnish such interference to healing. Tetany or a related condition, a disturbance of the vegetative nervous system, or a combination of both, are possible causes of the

supposed general overirritability. Patients with ulcer, with gastric neurosis, and controls were tested with various stimuli to ascertain the presence of such overirritable states. Almost all patients with ulcers respond excessively to mechanical, electrical and pharmacologic stimulation. Patients with gastric neurosis react similarly, except to mechanical stimuli, but present a marked contrast to the ulcer group in that they display obvious stigmas of a disturbed vegetative nervous system. This distinction may prove useful clinically. The persistence of the overirritability after a surgical cure suggests that it is a general bodily state, probably constitutional, and not merely the result of the presence of the ulcer.

S. A. Levinson.

Brain Repair. R. Wilson, Arch. Neurol. & Psychiat. **15**:81, 1926.

The author describes the appearance of needle tracks in two brains affected by general paralysis. In a recent case there was an intense cellular reaction of small round cells and gitter cells, with much cellular detritus. Connective tissue elements were seen proliferating in the canal. In older cases the connective tissue was more in evidence. The glia reacted by an increase in protoplasm. The repair of brain wounds is concluded to be done by connective tissue elements.

Roy Grinker.

A Contribution to the Pathology of Paralysis Agitans. C. M. Byrnes, Arch. Neurol. & Psychiat. **15**:407, 1926.

The author has studied the muscles and muscle spindles. He finds the muscle tissue essentially normal. In the spindles of fourteen cases, there was a constant lesion, beginning with edema and early degeneration of the intrafusal nerve. Later, there was disintegration of the entire spindle. No other disease has revealed this change. The author believes that the lesion is a toxic parenchymatous degeneration of the intrafusal nerve terminals.

Roy Grinker.

Gross Pontile Bleeding in Traumatic and Nontraumatic Cerebral Lesions. G. Wilson and N. Winkleman, Arch. Neurol. & Psychiat. **15**:455, 1926.

In thirteen cases of cerebral lesions of tumor, abscess, hemorrhage and traumatic hemorrhage, there were also multiple pontile hemorrhages which probably took place shortly before death. The pontile lesions probably account for the symptoms which have been ascribed to medullary edema. Increase in intracranial pressure from the primary lesion causing an impingement of the small pontile vessels on the base of the skull is the explanation of the pontile lesions.

Roy Grinker.

Pathologic Changes of Senile Type in Charcot's Disease. L. Van Bogaert and I. Bertrand, Arch. Neurol. & Psychiat. **16**:263, 1926.

In histopathologic studies of two cases of amyotrophic lateral sclerosis senila plaques were found in the brain. These are described in great detail.

Roy Grinker.

THE INFLUENCE OF DECOMPRESSION OPERATION ON EXPERIMENTALLY PRODUCED PAPILLEDEMA. L. DAVIS, Arch. Surg. **12**:1004, 1926.

The author was successful in producing experimental papilledema by introducing into the brain 2-grain (0.13 Gm.) gelatin capsules filled with agar. This foreign body closely simulates in its mechanism the action of cerebral tumors. His findings on thirty-five dogs may be summarized as follows: 1. The introduction of sterile agar into the cerebral or the cerebellar substance produces an increase in intracranial pressure which results in the production of papilledema. 2. The gradual increase in size of the agar due to its absorption of fluid closely simulates the mechanism of an intracranial new growth. 3. A subtemporal decompression opening prevents the occurrence of papilledema from the introduction of agar into the cerebrum or the cerebellum. Such a cranial opening is as efficient in the presence of a cerebellar tumor as is a suboccipital craniotomy. 4. The importance of the mechanical factor of an increase in intracranial pressure in the production of papilledema has been corroborated by this method.

N. ENZER.

INVOLUTIONAL OR REGRESSIVE CHANGES IN THE THYROID GLAND IN CASES OF EXOPHTHALMIC GOITER AND THEIR RELATION TO THE ORIGIN OF SO-CALLED ADENOMAS. W. F. RIENHOFF, JR., Arch. Surg. **13**:391, 1926.

Seven cases of fulminating exophthalmic goiter were studied. These cases had not been through any periods of remission, and control studies on the morphologic changes brought about by iodine therapy could be made. It is well established that patients with exophthalmic goiter go through repeated periods of remission and exacerbation and it has also been established that the administration of iodine brings about the clinical manifestations of spontaneous remission. In these cases Rienhoff removed a large portion of the right lobe and by serial sections established the microscopic picture of extreme hyperplasia. The patients were then given iodine and later a subtotal thyroidectomy was performed. By comparison the following features were established. The administration of iodine brings about an involution of the hyperplastic gland, which approaches the normal thyroid. The acini are dilated, the lining epithelium is flattened, the connective tissue is increased and the vascularity is decreased. The amount and density of the colloid is increased, and the lymphocytic infiltration is diminished. This is a uniform result. Two exceptions occur in the form of areas of hyperinvolution and hypo-involution. In the first there occurs localized cystic dilatation of acini which become surrounded by connective tissue. Such areas previously have been called colloid or cystic adenomas. The areas of hypo-involution are also localized or circumscribed and might also be termed areas of persistant or residual hyperplasia. Ewing termed these miliary adenomas. Clinically these are termed adenomas of the thyroid when found in cases of exophthalmic goiter which have passed through remissions; they may undergo subsequent changes in cases with recurrent hyperplasia of the whole gland. Such areas of hypo-involution must not be confused with the true parenchymatous or fetal adenomas.

N. ENZER.

THE TRANSPLANTATION OF BONE INTO JOINTS. S. L. HAAS, Arch. Surg. **13**:426, 1926.

Bits of bone encased in perforated rubber tubing were inserted into the knee joints of dogs and rabbits. These fragments eventually united by bone

formation and after from eight to nineteen days fibrous union took place to the synovial membrane. The foreign body did not cause any reaction in the knee joint.

N. ENZER.

ABSCESSES AND INFLAMMATORY TUMORS IN THE SPINAL EPIDURAL SPACE (SO-CALLED PACHYMENINGITIS EXTERNA). W. E. DANDY, Arch. Surg. **13**:477, 1926.

The existence of a dorsal epidural space from the seventh cervical to the first lumbar vertebra predisposes this area to infection. The space is filled with loose areolar tissue, fat and blood vessels. The infections may be acute or chronic, metastatic through the blood stream or due to direct extension. In the acute form an abscess develops, and in twenty-five cases collected in the literature all but two of the patients died. Apparently the vascular areolar tissue is able to respond to the infection with resultant abscess formation, for involvement of the whole epidural space is rare. The onset is acute with fever, leukocytosis and terrific pain at the level of the lesion and along the nerve trunks, followed in from four to nine days by motor, sensory and sphincter paralysis. The severe pain, tenderness and rigidity of the spine accompanied by a spinal subarachnoid block should suggest the diagnosis. The interval between the onset of pain and paraplegia is characteristic. In the chronic type the picture is the same except that it is chronic from the start, that is, slower onset with much less acute symptoms followed by a slowly developing paralysis. In these the pathology is that of a chronic inflammatory tumor, occasionally reported as syphilitic and tuberculous in nature. They frequently follow trauma and several have been reported which occurred after severe carbuncles in the skin over the area involved. In these inflammatory tumors the infecting organisms may be recovered and they are generally staphylococci. Three cases of the chronic type are reported by Dandy, who emphasizes that the condition is not pachymeningitis externa but an infection of the tissues in the epidural space.

N. ENZER.

THE VALVES OF HEISTER. S. H. MENTZER, Arch. Surg. **13**:511, 1926.

The author finds that in cadavers the valves of Heister do not impede the flow of fluid in the cystic duct in either direction. He concludes that they cannot be of great importance because of their absence in many animals and frequently in man, and that they probably control the rate of flow of bile from the gallbladder.

N. ENZER.

BRITTLE BONES AND BLUE SCLERA. HEREDITARY HYPOPLASIA OF THE MESENCHYME. J. A. KEY, Arch. Surg. **13**:523, 1926.

A 12 year old girl complained that her bones were easily broken. She had had thirty-three fractures. The family history was significant. The mother had blue sclerae, was deaf and had had two fractures. The grandmother and great-grandmother on the mother's side were deaf and had blue sclerae. Three brothers and two sisters had blue sclerae and three of the five had multiple fractures. The condition is familial and is transmitted by affected parents. Only those children with blue sclera are subject to brittle bones and persons so affected are generally small in stature. The blue of

the sclera results from an abnormal transparency of the sclerotic coat which permits the blue uvea to shine through. The deafness, which generally develops in adult life, is otosclerotic. Seventy per cent of persons with blue sclera have multiple fractures. These follow slight trauma and occur most frequently in childhood. The fractures are usually simple and occur generally in the shaft. It is characteristic that these fractures heal rapidly and well with little or no callous formation. Hypermotility of the joints, due to laxity of the fibrous supporting structures, leads to frequent sprains. The roentgenograms show the bone structure coarsened and the bone slender, and healed fractures frequently are not demonstrated. The bones are usually hard and brittle, honeycombed by large canals filled with vascular connective tissue and osteoblasts. The blood vessels, tendons, fascia and subcutaneous tissue are friable. The blood chemical observations are within normal limits. Idiopathic bone fragility may be classified thus: (1) hereditary form — hereditary hypoplasia of the mesenchyme; (2) nonhereditary osteogenesis imperfecta — (*a*) osteopsathyrosis with white sclera, (*b*) osteopsathyrosis with blue sclera; (3) osteosclerosis fragilis generalisata — marble bones.

N. Enzer.

The Effect of the Ligation of the Pulmonary Artery of One Lung Without and With Resection of the Phrenic Nerve. K. Schlaepfer, Arch. Surg. **13**:623, 1926.

Paralysis of the diaphragm by sectioning the phrenic nerve combined with ligation of the pulmonary artery causes much more pulmonary fibrosis than simple ligation of the artery, the formation of collateral circulation through the bronchial artery being retarded.

N. Enzer.

The Regeneration of the Lymphatics. F. L. Reichert, Arch. Surg. **13**:871 1926.

This study is the outcome of previous work done with the late Professor Halstead on the experimental production of elephantiasis. The procedure used was the replantation of a dog's hind limb. All of the tissues of the thigh including the periosteum were cut, leaving only the femoral artery, the vein and the bone, and these were carefully stripped of all surrounding areolar tissue. The muscle and skin edges were then carefully approximated by silk sutures. Several hours before the animal was killed diluted india ink was introduced into the foot-pads and into the skin of the leg and thigh distal to the operative line, and also into the popliteal lymph node. In some cases injections were made into the arterial system. The earliest observation of regeneration of lymphatics was four days after operation. It occurred in the superficial set of lymphatics at the line of skin division where healing occurred by primary intention. Where there was any appreciable scar or where healing was interfered with by trauma, foreign body or infection, the growth of lymphatics across that region was delayed weeks or months. Regeneration of deep lymphatics was first seen eight days after operation. In specimens in which the lymphatic infiltrations were made two, three and twenty weeks after the operation the main lymphatic trunk had frequently reunited, occasionally without any evidence of the point of division or else with an irregularity and kinking in the vessels at this point.

N. Enzer.

THE HISTOLOGICAL CHANGES BROUGHT ABOUT IN CASES OF EXOPHTHALMIC GOITRE BY THE ADMINISTRATION OF IODINE. WILLIAM FRANCIS RIENHOFF, JR., Bull. Johns Hopkins Hosp. **37**:285, 1925.

Iodine produces definite and striking changes in the histologic structure of the thyroid gland in cases of exophthalmic goiter.

These changes are as follows: (*a*) increase in size of the thyroid gland as a whole; (*b*) decrease in vascularity and probably in the lymph flow through the gland; (*c*) a large increase in amount of fibrous connective tissue; (*d*) a striking increase in amount of colloid deposited and contained within the thyroid gland; (*e*) a change in the acini from lacelike papillomatous ingrowths to round, even walled, smooth acini, regular in size and form; (*f*) a transition of epithelium from high columnar to flat cuboidal and occasionally low columnar; (*g*) a change in the nuclei of epithelial cells from large clear nuclei to the small irreguar pyckotic type; (*h*) the presence of many mitotic figures before the use of iodine and their absence after iodine has been given.

The clinical improvement and the lowered rate of basal metabolism are directly associated with the change from a typical histologic picture of exophthalmic goiter to a resting colloid state.

In comparing the histologic structure of the thyroid gland in thirty cases of exophthalmic goiter, fifteen in which iodine had been given and fifteen in which no medication had been used, it was observed that the histologic picture following the administration of iodine was constant and, compared with the microscopic structure of the glands in the case of patients not receiving iodine, corresponded exactly, as had the microscopic changes in the three cases in which an examination of the gland was made in each patient before and after the administration of iodine.

The colloid state is proved clinically and histologically to be less active than the hypertrophic and hyperplastic state.

An artificial remission is produced by iodine.

A remission in a case of exophthalmic goiter is associated with a change in the histologic picture from a hyperplasic to a colloid state, even though there is definite evidence of hyperplasia yet remaining. It is a question of a relative hyperplasia.

ATRETIC FOLLICLES IN THE OVARY OF THE RAT, MOUSE AND RABBIT, WITH SPECIAL REFERENCE TO THE SIGNIFICANCE OF THE BASEMENT MEMBRANE IN DETERMINING THE SOURCE OF ORIGIN OF THE INTERSTITIAL CELLS. W. V. WILKERSON, Bull. Johns Hopkins Hosp. **38**:339, 1926.

The interstitial cells are formed from the theca, particularly the theca interna, of atretic follicles and are, therefore, of connective tissue origin.

In the rat and mouse the interstitial cells are found as irregular groups scattered throughout the ovary and do not appear to have any definite arrangement, their position apparently being determined by the stress of growth changes within the ovary.

In the adult rabbit, the ovary is packed with interstitial cells, but these are not believed to be arranged in any special order or according to some definite plan.

In the rat and mouse the interstitial cells appear about the second week after birth, with individual variations, and are constantly present from this time on. They appear suddenly, becoming progressively more abundant as the animal approaches sexual maturity. Their number becomes much reduced after the period just preceding sexual maturity has passed.

The interstitial cells were first definitely recognized in the rabbit in animals 7 weeks old. They are constantly present from this time on, being most abundant in the adult animal.

The oocyte may degenerate without any marked changes, or it may undergo degenerative fragmentation, becoming broken up into numerous portions that have chromatin-containing nuclei, and these fragmentary cells disappearing. There is an unquestionable invasion of extra-ovular cells which are presumably connected in some way, possibly as phagocytes, with the final disappearance of the oocyte.

Fragmentation was not noted often in the rabbit, the process of degeneration being otherwise as in the rat and mouse.

A special or peculiarly close relationship to the blood capillaries or to the lymph vascular system could not be demonstrated.

The interstitial cells are not believed to constitute a gland of internal secretion.

AUTHOR'S SUMMARY.

THE LARGE MONONUCLEAR AND THE TRANSITIONAL LEUCOCYTE OF HUMAN BLOOD. F. A. MCJUNKIN, J. Lab. & Clin. Med. **12**:71, 1926.

The "transitional" leukocytes (monocyte of Naegeli) is the peroxidase reacting mononuclear phagocyte of human blood. It is one of the granular leukocytes of myeloid origin. When applied as a chemical test the peroxidase reaction permits the accurate differentiation of this cell from the nonperoxidase reacting phagocytes that have incorrectly been called monocytes. The second type of mononuclear phagocyte present in the normal peripheral blood is characterized by a focus of dye granules when the living cell is brought into contact with a dilute solution of neutral red. It is a nonperoxidase reacting cell which corresponds in its general structure to the leukocytes that have commonly been designated as "large mononuclears." Under experimental conditions, the third type of mononuclear phagocyte which is derived from the blood vascular endothelium may appear in the peripheral blood. By the method of supravital staining it may present a diffuse granulation or may be devoid of granules.

S. A. LEVINSON.

UNUSUAL CASE OF DEATH AFTER REMOVAL OF ADENOIDS AND TONSILS [HEMORRHAGE IN PONS]. H. BELL TAWSE, J. Laryng. & Otol. **41**:97, 1926.

The tonsils and adenoids were removed without special difficulty from a boy, aged 2 years and 8 months, under ethyl chloride anesthesia. The next morning, while sitting up to have his face washed, the boy fell back unconscious, and died within an hour. There was found a hemorrhage, the size of a large pea, in the center of the pons. All the other organs were normal.

THE CIRCULATION OF THE CEREBROSPINAL FLUID FROM THE STANDPOINT OF INTRAVENTRICULAR AND INTRASPINAL THERAPY. C. C. REQUIER and A. FERRARO, J. Nerv. & Ment. Dis. **64**:561, 1926.

The authors review the present theories as to the origin and circulation of the spinal fluid and present a large bibliography. They conclude that the fluid is carried from the ventricles to the subarachnoid spaces through the foramina of Luschka and Magendie, and also through the cerebral parenchyma. They believe that intraspinal therapy is of value because drugs penetrate the spinal parenchyma from the subarachnoid space and also are carried by an ascending current to the cerebral parenchyma.

ROY GRINKER.

CHRONIC ARACHNO-PERINEURITIS WITH THE SYNDROME OF DRAIN. REPORT OF A CASE WITH A DISCUSSION OF PSEUDOTUMOR SPINALIS. R. R. GRINKER, J. Nerv. & Ment. Dis. **64**:616, 1926.

Examination of a case clinically considered as a cauda equina tumor revealed only a chronic inflammation of the arachnoid about the lower portion of the spinal cord. The meningeal vessels were engorged and many were ruptured, to which fact the syndrome of Irvin was attributed. There were mild secondary degenerative changes in the root axones and the ganglion cells of the cord. Pseudotumor syndromes supposedly without pathologic evidence are shown to be due either to a radiculitis or to arachnoiditis.

AUTHOR'S ABSTRACT.

ASCARIS LUMBRICOIDES IN FALLOPIAN TUBE. H. E. MURRAY, J. Obst. & Gynec. Brit. Emp. **33**:448, 1926.

The extreme rarity of a round worm in the fallopian tube is described.

PHYSIOLOGIC ACTION OF LIGHT. II. DEPRESSION OF ARTERIAL BLOOD PRESSURE. III. EFFECTS ON ARTERIAL BLOOD PRESSURE OF DIRECT IRRADIATION OF BLOOD IN VIVO. IV. EFFECTS IN BLOOD OF IRRADIATION IN VIVO. C. J. REED, J. Physiol. **74**:511, 518, 525, 1925.

Reed found that a beam of light of approximately 100 f. c. intensity, when directed into one or both eyes of a dog under ether anesthesia will cause a pronounced depression of arterial blood pressure. A beam of light from a carbon arc employed in the same manner and giving a total intensity of 1,250 faradic current will produce a more profound depression of blood pressure. More intense light does not produce a change of proportionate magnitude but induces the same degree of change somewhat more rapidly. This effect is not wholly due to nervous factors since bilateral vagisection and section of the optic nerve do not abolish or prevent the effect, although the latter operation does modify it considerably. No positive evidence was obtained that photochemical decomposition liberated any depressor substance into the blood stream. Short ultraviolet rays were not present in either of the two sources of light employed.

Reed states that direct irradiation of blood circulating through a quartz tube interposed in an artery will cause a massive depression of general arterial blood pressure. Animals sometimes die from the shock even when anesthesia has been discontinued. This result may be obtained in irradiation with a carbon arc rich in ultraviolet or with a spectrum from which infra-red rays have been filtered (longer than 7,000 Angström units) or ultraviolet rays below 3,300 Angström units. The differences between results obtained with these three spectrums are not pronounced.

A beam of light of approximately 4,000 faradic current intensity projected from the positive electrode of a carbon tungsten arc lamp operated on a 110 volt direct current circuit at 4 amperes and condensed through a quartz lens was directed by Reed on a quartz tube interposed in the carotid artery so that the blood flowing through the tube was irradiated directly. Minor changes in hemoglobin percentage and in erythrocyte count occurred in both irradiated and control dogs to about the same degree so that it is probable that the increase was due to concentration of the blood. There was an absolute leukopenia, a lymphopenia but a relative lymphocytosis. The changes were not due to the anesthetic or to shifting of leukocytes. All available evidence indicates that

photodynamic effects are, biologically, stimulators of oxidation; and it is suggested that rays constitute one means of accelerating metabolism, which may, however, proceed to a degree of intensity that is destructive.

PELVIC HERNIA. L. M. MILES, Surg., Gynec. & Obst. **42**:482, 1926.

The literature of vaginal hernia is reviewed, nine cases being definitely classified as such; to these the author adds two of his own. Twenty-five authentic cases of perineal hernia were collected by Moschcowitz in 1912, and Chase recorded thirteen cases of pudendal hernia in 1922. Vaginal hernia is traumatic in origin, usually following pregnancy or child-bearing. The author offers a new classification embracing all hernias through the pelvic floor, for which the name "pelvic hernia" is proposed as an inclusive term, the point of egress of the hernia being added to designate the subvariety. Thus pelvic hernia may be perineal, pudendal or vaginal; and vaginal hernia may be anterior or posterior. Prolapse of the uterus accompanied by general enlargement of the cul-de-sac and protrusion of the abdominal contents into the vaginal vault should be called vaginal enterocele and not hernia. The treatment is operative; the best operation is by the perineal route, excision of the sac and repair of the perineum being combined with an abdominal operation for obliterating the cul-de-sac.

M. L. PARKER.

RUPTURE OF AORTA INTO PERICARDIAL SAC. E. T. GALLAGHER, U. S. Vet. Bur. M. Bull. **2**:972, 1926.

A patient with aortitis and aortic regurgitation was taken down with influenza and died suddenly sitting in bed. There was a rupture of the aorta through an atheromatous area just above the valves.

EPILOIA. T. BRUSHFIELD and W. WYATT, Brit. J. Child. Dis. **23**:178, 1926.

Sixteen cases of the syndrome of mental deficiency, epilepsy, adenoma sebaceum, nodular sclerosis of the cerebral cortex and renal and other tumors are analyzed. Sherlock named the condition epiloia.

BILATERAL RENAL ANEURYSM. F. H. HEALY, Brit. M. J. **1**:374, 1926.

In the case cited by Healy, aneurysms were found on both renal arteries. The right artery was tortuous and presented a firm swelling, the size of a tangerine, at the entrance of the hilum. Three swellings, the size of peas, were present on subdivisions of the artery. The left artery had swellings in the same position, but on a slightly smaller scale. The aneurysmal dilatation of the renal vessels was a sequel to arteriosclerotic changes. The heart showed marked concentric hypertrophy of the left ventricle, and atheroma of the coronary arteries. The brain showed sclerosis of all arteries, particularly of the basal. Three old hemorrhages were present: the oldest, in the right internal capsule; the intermediate, in the left internal capsule; and the most recent, just anterior to the genu of the left internal capsule.

THE FATE OF THE GRAAFIAN FOLLICLE IN THE HUMAN OVARY. W. SHAW, J. Obst. & Gynec. Brit. Emp. **32**:679, 1925.

Since the child bearing age is about 36 years, only 500 follicles can be accounted for by ovulation and subsequent corpus luteum formation. The rest of the total, estimated by Marshal to be about 100,000 and by Stevens 10,000, must disappear by the process of atresia. During the postmenstrual

period, from 8 to 10 ripening follicles can be found. Study of very early corpora lutea has shown that the theca interna becomes very vascular, and that its cells become transformed into paralutein cells. The granulosa cells of the follicle undergo extreme hypertrophy, grow centripetally and develop into large lutein cells; they form the main part of the corpus and give rise to the internal secretion. The proliferative phase occurs during the 16th to 19th day of the menstrual cycle, the mature corpus luteum being gray. Degeneration of the corpus luteum of menstruation is seen the day prior to the menstrual discharge. The cells of the theca interna and the large lutein cells become vacuolated by the presence of fatty acids, and the body takes on the yellow color which has given it its name. Shaw believes it is rare for hemorrhage to occur into the cavity of the young corpus luteum following rupture of the follicle; hemorrhage may occur in certain pathologic conditions in which hyperemia prevails. In the process of degeneration, hyaline substance is deposited between the cells and in the cavity. This compresses the lutein cells and atrophy follows. The cavity persists, but is greatly reduced in size; a tortuous ring of hyaline tissue is formed, and the corpus albicans is the end result. In previous work the author has calculated that about eight months are required for conversion of a corpus luteum into a corpus albicans. In the follicles which do not go on to ovulation, atretic processes take place. The cells of the theca interna hypertrophy centrifugally and assume a brown color like that of the lutein cells. The vascularity is steadily diminished, and fatty changes may be noted. The granulosa cells undergo degeneration, fatty acids soon appear in the protoplasm, and the cells shrink and disappear. Between the layers of granulosa and theca cells, the so-called glassy membrane of hyaline tissue appears. The corpus atreticum is thus formed. The latter collapses, forming an irregular, hyaline body of wavy bands having no central cavity, and a corpus candicans results. When hyaline tissue from the glassy membrane invades the atretic follicle, an ovoid structure which does not collapse is formed, and this is known as a corpus fibrosum. The atretic process occurring in the smaller, and even in the primordial, follicles, results in thin, wavy strands of hyaline tissue; these are the restiform bodies.

A. J. KOBAK.

ON THE SO-CALLED CALCIFICATION IN THE BASAL GANGLIA OF THE BRAIN. E. WESTON HURST, J. Path. & Bact. **29**:65, 1926.

The author observes that "calcification" affecting the arteries in the globus pallidus of the lenticular nucleus is found so frequently in cases of paralysis agitans, both in the idiopathic and the postencephalitic forms of the disease, that its occurrence would seem to be a constant feature of these cases.

One hundred brains were examined by the author, and deposits in the vessels of the globus pallidus were observed in 50. Arterial deposits were seen in all 7 cases of paralysis agitans, in 3 of 5 cases of encephalitis, in 4 of 7 cases of cerebral vascular disease, in 17 of 29 cases of cerebral tumors, etc. All age periods were affected from 20 to 81 years.

The deposit may occur chiefly in the media of the arteries, or it may primarily affect the adventitia and spread to the media later. The process consists in an infiltration of one or more coats of the vessel with finely granular substance which stains brown, brownish purple or blue-black with alum hematoxylin and van Gieson stain, and has therefore been regarded as calcium. The author was unable to demonstrate calcium by means of microchemical tests, but found iron salts constantly present.

Degeneration bodies also frequently infiltrated with iron were found in the globus pallidus in 68 per cent of the cases and in the putamen in 30 per cent.

The author believes that the presence of these vascular deposits and of degeneration bodies is an expression of the proclivity of the affected regions to undergo degeneration in the second half of life. The deposition of iron salts is to be correlated with the high iron content of these parts of the brain.

E. M. HALL.

PNEUMATIC CYSTS OF LYMPH VESSELS. P. MASSON, Ann. d'anat. path., Med.-chirurg. **2**:54, 1926.

The accumulation of gases under pressure within lymph vessels which dilate into the true cysts with endothelium varying from nearly normal to a greatly thickened plasmodial layer on a proliferative connective tissue base, has been observed in many species. In human beings cysts of the vaginal wall of pregnant women were first described; later similar cysts were found in the intestinal walls and adjacent mesentery, most common in the ileal portion, about the cecum and ascending colon, exceptionally in the omentum and stomach wall but not about the transverse or descending colon. They may be submucous or subserous, may contain more or less fluid, do not cause erosion of the overlying membrane, and are most numerous near the line of the mesenteric attachment or within the mesentery itself.

Within the cysts nitrogen (73 to 90 per cent) and oxygen (5 to 20 per cent) are always present, carbon dioxide varies from 0 to 15 per cent and traces of hydrogen and methane are sometimes found. This composition differing from that of the intestinal gases is evidence against the direct absorption or the mechanical propulsion of such gases through the mucous membrane. The frequency of cysts in hogs fed on dairy products and in human beings with ulcer of the stomach or duodenum or other gastro-intestinal conditions leading to an increase of the acidity (lactic acid) of the intestinal contents further suggests that carbon dioxide held by acid is absorbed in concentrations higher than usual and then freed by neutralization within the lymph; accumulation and diffusion with the other gases of the blood and lymph then follow, according to the laws for diffusion of gases as governed by the existing anatomic and physiologic conditions. So long as the inciting factors persist, new cysts may be formed, and the older ones resorbed to leave sclerosed tissue. The cure sometimes following laparotomy may be due to the inflammatory changes, with the resultant variation in the chemical balance.

ETHEL B. PERRY.

THE INCIDENCE AND THE PROCESS OF CALCIFICATION IN GLIOMAS OF THE BRAIN. ARTHUR VAN DESSEL, Arch. franco-belges de chir. **28**:845, 1925.

This is a report of work in Dr. Cushing's clinic in the Peter Bent Brigham Hospital in Boston. The author concludes that an exact topographic diagnosis of glioma of the brain can be made in a certain number of cases because of the presence of calcareous deposits in the tumors. Such calcifications are demonstrable with increasing frequency following improvements in roentgenographic technic. Calcification is found in a variety of tumors of different cellular structure. The calcium salts are deposited almost exclusively in the walls of the vessels, the seat of hyaline degeneration.

FATTY METAMORPHOSIS OF THE TWO SUPRARENAL CAPSULES WITH MELANODERMA. M. LOEPER and J. OLLIVER, Bull. et mém. Soc. méd. d. hôp. de Paris **50**:312, 1926.

A woman, aged 31, died after having suffered from a disease that resembled in every way Addison's disease, including marked bronzing of the skin. The suprarenals each appeared to be reduced to a mass of fat, and it is suggested that there may have been a congenital malformation. There was no sign of tuberculosis in the suprarenals.

HEMORRHAGIC PACHYMENINGITIS IN INFANTS. R. DEBRÉ and G. SEMELAIGNE, Presse méd. **34**:337, 1926.

The authors report five certain and two probable cases of hemorrhagic pachymeningitis in infants, seen in one year. The usual age is 2 to 6 months. The onset is insidious, with weakness, insomnia, anorexia, and indefinite nervous symptoms, but occasionally is sudden with high fever and convulsions. Hydrocephalus is one of the earliest signs. The diagnosis is made by puncture of the ventricle and ophthalmoscopic examination. The fluid is under increased pressure, red or yellow, and after it has stood, red blood cells separate out. Cultures are sterile. The fluid from the spinal canal is normal or merely yellowish. In about half of the cases there are retinal hemorrhages. The course is usually subacute, and the patients that do not die of intercurrent events make a gradual recovery. A few die of the meningitis itself, usually the acute form. Sequelae sometimes remain. The essential lesion seems to be the formation of a false membrane, with secondary hemorrhage from the altered vessels. Signs of congenital syphilis are present in many cases. Antisyphilitic treatment is advised, with ventricular puncture, injection of coagulants, and occasionally cerebral decompression.

B. R. LOVETT.

THE PREDILECTION OF THE APEXES FOR TUBERCULOSIS. H. LOESCHCKE, Beitr. z. klin. Tuberk. **64**:455, 1926.

The tertiary phthisis begins most frequently in the area of the dorsal apical and subapical bronchus. This is true at least for the phthisis of adults. On the basis of pathologic-anatomic studies, the author attempts to explain this predilection by the traction which is exerted on these parts by mere gravity and by the diaphragmatic movements. This causes stretching of blood and lymph vessels in these parts since the periodic respiratory motions exert a traction which is in inverse proportion to the horizontal diameter of the organ. This effect may be constitutionally increased in the asthenic type. The apexes are more exposed to vertical traction on account of their smaller dimensions, the lack of muscular tonus, and the deficiency of proper support for the abdominal organs on account of the scarcity of intra-abdominal fat tissue. It may be conditionally and only temporarily increased by any weakening or emaciating disease. This conception would explain why the predisposition of the apexes is not found in children and in certain anomalies of the vertebral column.

MAX PINNER.

BRONCHIECTASES OF THE PRETERMINAL BRONCHIAL SYSTEMS. H. LOESCHCKE, Beitr. z. klin. Tuberk. **64**:382, 1926.

A case is described of a 43 year old man who suffered for about twelve years from a purulent bronchitis with asthmatic attacks. The necropsy showed

generalized bronchiectases of the small bronchi with partial destruction of the muscular and elastic layer. The multiple small cavities are believed to correspond to caverniculae (Brauer) in the roentgenogram.

MAX PINNER.

THE TOPOGRAPHY OF THE BRONCHIAL LYMPH NODES AND THEIR ANATOMIC DEMONSTRATION. S. ENGEL, Beitr. z. klin. Tuberk. **64**:468, 1926.

A careful anatomic study led to the establishment of the following groups of lymph nodes: (1) lymphoglandulae bifurcationis dextrae et sinistrae; (2) lymphoglandulae tracheobronchiales dextrae; (3) lymphoglandulae hilares anteriores dextrae; (4) lymphoglandulae hilares posteriores dextrae (interlobares); (5) lymphoglandulae hilares anteriores sinistrae; (6) lymphoglandulae hilares posteriores sinistrae (interlobares); (7) lymphoglandulae aortae; (8) lymphoglandulae ductus botalli.

MAX PINNER.

THE RÔLE OF THE RETICULUM IN THE RETICULO-ENDOTHELIAL SYSTEM. K. PASCHKIS, Centralbl. f. allg. Pathol. u. path. Anat. **37**:99, 1926.

From regular frozen and shake preparations of lymph glands of rabbits injected intravenously with lithium carmine; from observations on the size of dye granules in the Kupffer cells, sinus epithelium of the spleen and in bone marrow; from the demonstration of siderosis in lymph sinus reticulum and in some cases in the reticulum of adenoid tissue in cases of pernicious anemia, and from observations on cell morphology, the author concludes that the reticulum and endothelium form a morphogenetic, closely related, cell group. Under certain circumstances, functional differences occur, but how much these are dependent on hematogenous or how much on lymphogenous factors, he cannot decide.

GEORGE RUKSTINAT.

COMPENSATORY COLLATERAL CIRCULATION IN A CASE OF CONGENITAL PULMONARY STENOSIS. W. ARNOLD, Centralbl. f. allg. Pathol. u. path. Anat. **37**:193, 1926.

The collateral circulation consisted of a superior bronchial artery arising from the concave part of the aortic arch, a branch of the left subclavian artery, a posterior bronchial artery springing from the descending part of the aorta and two arteries probably coming from the inferior thyroid artery. Between these vessels there were numerous anastomoses. The right lung was ultimately supplied by four arteries and the left by three.

GEORGE RUKSTINAT.

AN ACCESSORY LIVER WITH CIRRHOTIC CHANGES. R. BRÜHL, Centralbl. f. allg. Pathol. u. path. Anat. **37**:245, 1926.

A "bean-sized" accessory liver was found in the great omentum near the greater curvature of the stomach in a 16 year old girl dying with cirrhosis of the liver. Microscopically the anomalous mass contained disordered cords of liver cells with an abundance of bile pigment; collagenic connective tissue strands emanating from the capsule and blood vessels; bile cysts; necrotic places and round and polymorphonuclear cell infiltration. No fat or iron were demonstrable. An anatomic reconstruction was impossible, but the author thinks ducts for carrying away the bile existed and later became occluded, so that the bile cysts resulted.

GEORGE RUKSTINAT.

THE ACTION OF THE ROENTGEN RAYS ON PROTOPLASMIC STRUCTURE DURING THE SO-CALLED "LATENT" PERIOD. S. S. WAIL and J. G. LIBERSOHN, Centralbl. f. allg. Pathol. u. path. Anat. **37**:247, 1926.

One kidney area in rabbits was exposed to roentgen rays, and the other was screened for a control. In the latent period, before nuclear disintegration began, protoplasmic changes were not demonstrable in the convoluted tubules by hematoxylin and eosin or Giemsa stains. Using Snessareff's modification of Altmann's mitochondria stain, globular bodies instead of rodlike structures were found in the cells in the latent period.

GEORGE RUKSTINAT.

AMYOTROPHIC SPINAL SYPHILIS. T. FALKIEWICZ, Deutsche Ztschr. f. d. Nervenh. **89**:230, 1926.

A case of tabes with muscular atrophy is reported which histologically revealed syphilitic meningeal infiltration about the cord with secondary involvement of the marginal nervous tissue most marked in the anterior portion. The author believes his case agrees with the theory that the chronic meningitis is the pathogenesis of tabetic cord pathology.

ROY GRINKER.

LOCAL AMYLOIDS OF THE URETHRA. A. VON ALBERTINI, Frankfurt. Ztschr. f. Path. **33**:248, 1925.

Although general amyloidosis is found relatively often at necropsy, local amyloid, with the exception of amyloid of the larynx, is rare. The chemistry and origin of the amyloids are obscure. Neuberg believes that amyloids of different descent are different substances, and steps in the development of true liver amyloid, which is the goal they all tend to reach. According to his idea, albumin remnants, in great part diamino acids, are the principal carriers of the peculiar color reaction of amyloid and not as formerly thought the chondroitin-sulphuric acid, which according to Hansen and Eppinger is not a constant constituent of the amyloids.

Leupold was the first to apply colloid chemistry to the study of amyloids. He considers them gel substances existing as emulsion colloids, and he observes that paired sulphuric acid in the organs plays a great rôle. Increased quantities of paired sulphuric acid cause the appearance of iodine-reacting amyloids. The methyl violet reaction he believes is also determined by the presence of paired sulphuric acid. Leupold holds that chronic suppuration causes the formation of albumin bodies, which become deposited in the organs through the presence of increased quantities of sulphuric acid.

In regard to the formation of local amyloid, von Albertini discusses two possibilities, (1) that the deposition of amyloid mother substance in a given organ from that circulating in the blood is caused by the retention of paired sulphuric acid in that particular organ; (2) that the amyloid mother substance is formed and stored as amyloid within the organ. Bender believes that the latter process may be brought about by infectious toxic processes; von Albertini agrees with Leupold and Bender that the process is entirely local, according to the second possibility.

Local amyloid is most frequently found in the larynx, nose, trachea, bronchi and lungs. Many cases of amyloid of the tongue are found, next in frequency it occurs in the heart, intestine, liver and ribs. Rarely has amyloid been found in the urogenital tract. Only two cases of amyloid of the bladder and two cases of amyloid tumor of the urethra are known, the present one making the

third. This case occurred in a man, aged 72, who had had gonorrhea forty-eight years previously, and who had for five years suffered from bladder trouble. Following improvement of the bladder symptoms, there was increasing difficulty in urination. The urethra was enlarged to the size of the little finger and was hard. The tumor, which was located in the pars scrotalis, measured 5 by 4.5 by 2 cm. There was a marked chronic inflammation of the urethra extending well through the wall. In the thickened wall lay many clear masses, partly as nodules, partly as narrow solid strands which appeared as scalelike cross striations. In between the clear masses were atrophied strands of connective tissue. The clear areas stained light red with eosin, yellow with van Gieson stain. The methyl violet and methyl green reactions were not satisfactory, but the iodine reaction gave much better results. In the peri-urethral tissues the amyloid was found only in the walls of the arteries. In the immediate vicinity of the amyloid masses were numbers of foreign body giant cells which contained masses of amyloid. It is suggested that the amyloid in this case may have resulted from the gonorrhea.

E. M. HALL.

LIPOIDS AND PIGMENT IN THE UPPER RESPIRATORY MUCOSA. H. MITSUHASHI, Virchows Arch. f. path. Anat. **261**:1, 1926.

As a contribution to the normal and pathologic distribution of lipoids in human tissues, Mitsuhashi, at the suggestion of Lubarsch, investigated the occurrence of lipoids and pigment in the mucosa of the nose, larynx and trachea in 200 patients varying in age from fetuses to the seventieth year. At all periods adipose tissue is present in the mucosa in the situations studied, except in the nose. In the normal mucosa of children and adults phosphatids are present in the cells of the mucous glands. These phosphorus-containing lipoids increase in chronic metabolic disease and in diseases associated with cachexia. They are not increased in tuberculosis if cachexia is absent. In local inflammatory conditions the macrophages contain anisotropic phosphatids. Metabolic pigment appears early in life in the smooth muscle cells and increases with age. It becomes greater in amount in chronic metabolic and cachectic diseases but the increase is not parallel to that of the phosphatids in the same conditions. The intracellular formation of lipoids in vitro in the explanted respiratory mucosa of the rabbit was found to be dependent on the composition of the medium.

O. T. SCHULTZ.

LIPOID NEPHROSIS. K. LÖWENTHAL, Virchows Arch. f. path. Anat. **261**:109, 1926.

In two cases the clinical course was such as the author considers characteristic of lipoid nephrosis, namely gradual onset, slow course with periods of improvement, marked albuminuria with the presence of doubly refractile lipoids in the urine, and decreased urine and chloride output and edema in the terminal stage. Hypertension, cardiac hypertrophy, nitrogen retention and uremia were absent. The kidneys were enlarged and pale, the tubules were dilated and the tubular epithelium was filled with lipoids. The author attempted experimentally, by feeding cholesterol to rabbits, to establish his hypothesis that the disease is primarily a disturbance of lipoid metabolism, the kidneys at first merely excreting the excessive lipoids of the blood but finally themselves becoming pathologically altered. In the experimental animals hyperlipoidemia and grossly detectable lipemia resulted. Renal changes developed which were similar to those seen in the human kidneys. Lipoid excretion

in the urine preceded the excretion of albumin, evidence that the kidney is not damaged at this stage but that the urinary abnormality is the result of the adaptation of the secretory activity of the kidney to the altered composition of the blood. Although some of the manifestations of human lipoid nephrosis, such as edema, cannot be produced in the rabbit, the author concludes as the result of his clinical and experimental study that lipoid nephrosis is one of the secondary manifestations of a primary abnormality in lipoid metabolism.

O. T. SCHULTZ.

UNUSUAL BLOOD DISEASES. F. HOFF, Virchows Arch. f. path. Anat. **261**:142, 1926.

On the basis of a rich necropsy and clinical material, Hoff describes some unusual hematologic diseases and discusses the relationship of several types of blood disease to each other and to infection. In two cases of clinically acute myeloid leukemia with sepsis, characteristics of pernicious anemia were present, namely, poikilocytosis and anisocytosis with the presence of megalocytes and megaloblasts, achylia and hemosiderosis. The sepsis was not believed to have been an essential factor in the leukanemic blood picture. Two cases of monocytic leukemia led Hoff to conclude that monocytes in pathologic conditions of the blood may be myeloid or lymphoid in origin or they may come directly from the reticulo-endothelial system, a trialistic origin which will satisfy neither the monists or the dualists but would seem to cover all theoretical possibilities. The occurrence of megaloblasts in the peripheral blood is not limited to pernicious anemia. In addition to their presence in the two cases of acute myeloid leukemia noted previously, they were observed in a case of infantile von Jacksch anemia which followed the use of goat's milk and in which cure was effected by proper dietary measures. The occurrence of severe anemias, sometimes of the pernicious type and sometimes of the hemolytic icterus type, in association with syphilis, causes the author to believe that syphilis is an important etiologic factor in diseases of the hematopoietic system.

O. T. SCHULTZ.

PATHOLOGIC ALTERATIONS OF ARTERIES OF THE UPPER EXTREMITY. MARGARETE HESSE, Virchows Arch. f. path. Anat. **261**:225, 1926.

Margarete Hesse, working in the laboratory of Anitschkow, who has devoted much of his attention to arteriosclerosis, made a systematic study of the arteries of the upper extremity, from the subclavian to the radial artery, in forty-one necropsies of subjects varying in age from 2 days to 79 years. A normal gross anatomic characteristic of the portion of the arterial system studied is the transformation of the thicker, elastic type of artery into the thinner, muscular type at the level of the superior border of the pectoralis major muscle. At the region of the elbow the brachial artery is normally somewhat wider than just above this situation, its course is more tortuous, its wall is less elastic and its intima is somewhat uneven. The media here is usually richer in ground substance and connective tissue than elsewhere and many of the muscle fibers do not take an even, circular course. In younger persons the length of the main arterial stem of the upper extremity underwent a shortening of about 40 per cent of its length on removal, whereas in older persons the shortening was slight. Atherosclerotic changes characterized by fatty change but without calcification were almost the rule in the subclavian and axillary subdivisions in persons above the fourth decade. Beyond the point of transition of the

vessel from the elastic to the muscular type lipoid infiltration was only slight, localized calcified plaques were rare, but diffuse calcification of the media was much more marked and increased distally, being greatest in the radial and ulnar divisions.

O. T. SCHULTZ.

EXPERIMENTAL STUDY OF THE CHROMOTROPIC GROUND-SUBSTANCE OF THE ARTERIAL WALL. A. SSOLOWJEW, Virchows Arch. f. path. Anat. **261**:253, 1926.

Recent work has ascribed to the so-called chromotropic ground-substance of the arterial wall an important rôle in the pathogenesis of arteriosclerosis, since lipoid infiltration and fibrosis appear to occur earliest in this constituent of the vessel wall. The mucoid character of the ground substance is normal for the artery wall, and the presence of the chromotropic material is not an evidence of mucoid degeneration. The material is relatively increased with advancing age, but whether it undergoes a physical chemical change leading to swelling or is actually increased in amount is a moot question. The author studied the behavior of the ground-substance of the regenerating arterial wall. The procedure finally adopted consisted of injuring the outer surface of the wall of the carotid arteries of dogs by means of a hot metal wire, the vessel being removed and examined microscopically at periods varying from one hour to 127 days after the injury. During the first twenty-four hours the endothelium and muscle cells in the injured area disappeared, the elastic tissue became broken and was reduced in amount, the ground substance became fibrillated and its chromotropism was decreased. By the sixth day the chromotropic property had disappeared completely. Regenerative changes made their appearance at the margins of the injured area on the third day; they consisted of proliferation of endothelial and muscle cells and an increase in chromotropic substance. The latter made its way in the form of somewhat tortuous processes into the injured area, the proliferated muscle cells following these processes. The chromotropic material took part in the new formation of collagenous and elastic fibrils. The author concludes that the material is a product of the normal regenerating cells, that it takes an important part in the phenomena of regeneration and that its increase is an evidence not of degeneration but rather of proliferative activity.

O. T. SCHULTZ.

FUNCTION OF THE INTERSTITIAL TISSUE OF THE TESTIS. W. S. SIMNITZKY, Virchows Arch. f. path. Anat. **261**:265, 1926.

The rôle of the interstitial tissue, which is increased after degeneration, atrophy and disappearance of the seminal tubular epithelium following ligation of the vas, replacement of the testis in the peritoneal cavity and a variety of other procedures, is still a matter of dispute. That there is an actual rather than a relative increase appears doubtful, although the rejuvenation work of Stenach, Woronoff and others was based on the conception that the interstitial tissue actually increases in amount and exerts an increased internal secretory formation of sex hormones. Since deficiency in vitamin B leads to decrease in the size of the testis of pigeons, with degeneration of the tubular epithelium, the author chose this method of bringing about the changes in the testis which he desired to study. The avitaminosis of his birds was associated with progressive decrease in the size of the testis, due to degeneration and fatty change of the tubular epithelium in the earlier stages and removal of the degeneration products and shrinkage of the tubules in later stages. The interstitial tissue occupied a larger proportion of the substance of the testis, the increase being

due not merely to the decrease in the size of the tubules but also to actual increase of the size of the individual cells of the interstitial tissue. Active multiplication of the cells was not apparent. The hypertrophy of the cells was due to their saturation by lipoid material which was derived from degenerated tubular epithelium. The lipoid infiltration of the interstitial cells was always proportional to the degeneration of the tubules. The author concludes that the interstitial tissue is a trophic organ which has the function of furnishing the tubule cells necessary products and removing from the cells the products of degeneration, lipoid substances being important in both processes.

O. T. SCHULTZ.

ASEPTIC NECROSIS OF BONE. E. FREUND, Virchows Arch. f. path. Anat. **261**:287, 1926.

The author describes in detail the microscopic changes in the bone in a case of bilateral aseptic necrosis of the head of the femur, stressing his observations because of their similarity to those which occur in Perthe's juvenile osteochondritis deformans, Köhler's disease of the metatarsals, Kienböck's malacia of the semilunar bone and König's osteochondritis dissecans of the knee joint. Two years before her death the patient, a woman, aged 77, had suffered a fall. The injury was followed by constant pain in both hip joints and by inability to walk from that time on. There was no fracture of the neck as determined by roentgenographic examination. At necropsy evidence of previous fracture was not found. The cartilage covering the convexity of the head was irregular. The underlying bone trabeculae were necrotic and partly absorbed, and the fatty marrow contained droplets of oil and osseous detritus. There was no cellular infiltrative reaction. The deeper margin of the necrotic area was bounded by a rather wide zone in which the fatty marrow had been replaced by granulation tissue which in some places was dense and in other places cellular. Partial absorption of bone trabeculae had occurred in this zone. This encapsulating zone prevented complete removal of the necrotic material. The irregularity of the covering cartilage was secondary to the shrinkage of the underlying necrotic bone. The author believes that the necrosis probably resulted from the injury of numerous small blood vessels by the trauma of the fall.

O. T. SCHULTZ.

CONCERNING THE SO-CALLED "DIFFUSE BRAIN SCLEROSIS." W. WEIMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:411, 1926.

In a case of diffuse sclerosis the author found a symmetrical softening of both occipital lobes extending into the parietal and temporal lobes. Microscopically there was complete demyelinization with severe damage to the axones and the formation of a great quantity of lipoid products within gitter cells and atypical glia cells. There were occasional lymphocytic infiltrations bordering the softening and the formation of a thick central glia fiber net.

ROY GRINKER.

THE PATHOLOGIC ANATOMY OF THE CHRONIC FORM OF EPIDEMIC ENCEPHALITIS. L. OMOROKOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:421, 1926.

In the two reported cases special damage at the subcortical ganglion was not observed nor were vascular changes or infiltration found. There was a severe ependymitis without glial proliferation. Certain inclusions in the

ependymal cells resembled parasites. Ganglion cell changes were most severe in the cortex and about the ventricles, and were peculiar in that the nucleoli were vacuolized.

ROY GRINKER.

THE GLIA SCAR IN RHOMBENCEPHALON AND DIENCEPHALON FOLLOWING ENCEPHALITIS EPIDEMICA. W. HOLZER, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:503, 1926.

Thick glia fiber network was found about the inferior olive and the periventricular nuclei. Glia fibers were increased about all the vessels.

ROY GRINKER.

PATHOLOGIC ANATOMY OF CYSTICERCUS OF THE BRAIN. W. LASAREW, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:667, 1926.

Parasites were found in the brain surrounded by a layer of epithelioid cells, a layer of connective tissue and an outermost layer of round cells. There was an adventitial hyperplasia of the vessels which were surrounded by a thick layer of collagenous tissue. Many master glia cells were noted.

ROY GRINKER.

THE DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF CYTOLOGIC EXAMINATIONS OF THE SPUTUM. R. ENGELMANN, Ztschr. f. Tuberk. **44**:373, 1926.

Two distinctly different types of cells, carrying pigment, may be found in sputum. The larger ones, with a definite nucleolus, are considered to be alveolar epithelial cells; the origin of the other type is not known. Alveolar epithelial cells were found in about 50 per cent in the sputums of clinically healthy persons and in 67 per cent of tuberculosis sputums, more frequently in mucoid than in purulent material and more frequently in bacilli negative sputums. The author concludes that bacillus negative sputum that does not contain any alveolar cells must be suspected as not coming from the pulmonary tissue, and that only a negative sputum which contains alveolar cells is conclusive.

MAX PINNER.

ON THE INFLUENCE OF INHALATION OF COAL DUST ON THE FORMATION OF CONNECTIVE TISSUE IN THE LUNGS. K. HENIUS and O. RICHERT, Ztschr. f. Tuberk. **46**:123, 1926.

Rabbits which were exposed to the inhalation of coal dust simultaneously with a subcutaneous infection with bovine tubercle bacilli did not show more production of connective tissue than control animals. The pigment was found rather evenly distributed throughout the lung, deposited chiefly in cells of the alveolar septums, and in numerous alveolar epithelial cells. There was a slightly denser accumulation around some of the tuberculous foci.

MAX PINNER.

ON THE EFFECT OF LIPIODOL [IODIZED OIL] ON THE MENINGES. A. F. LINDBLOM, Acta Radiol. **5**:129, 1926.

Subdural injections of relatively large quantities of an organic combination of iodine and oil of white poppy which injected into the bronchi does not seem to cause any irritation, into rabbits gave rise to acute leptomeningitis, evidenced histologically by an extensive infiltration of cells (mainly leukocytes). It subsided in two or three weeks. In one case of seven it resulted in death.

After the period mentioned no histologic changes remain, in spite of remaining large quantities of the drug. After intralumbar injection (5-10 cc.) in man, acute leptomeningitis develops with marked increase of cells in the lumbar fluid (exclusively lymphocytes). The meningeal symptoms have subsided within two weeks after the injection.

AUTHOR'S SUMMARY.

DUODENOJEJUNAL DIVERTICULUM. A. KROGIUS, Finska läk.-sällsk. handl. **68**:835, 1926.

Sudden intestinal obstruction in a woman, aged 64, was caused by a duodenojejunal diverticulum buried in fibrous adhesions.

CONGENITAL ANEMIA WITH ERYTHROBLASTOSIS. E. L. FRANK, Nederl. Tijdschr. v. Geneesk. **2**:1384, 1926.

The patient died with severe anemia thirteen days after birth. Myeloid tissue was found in liver and spleen.

CHANGES IN THE SUPRARENALS IN ADDISON'S DISEASE. F. HARBITZ, Norsk Mag. f. Lægevidensk. **87**:371, 1926.

The author has examined the suprarenals carefully in 22 instances of Addison's disease. In 20 of the cases tuberculosis with caseation, replacing practically the whole substance of each gland except small remnants of cortex, was found. In two of the cases there was chronic inflammation with atrophy of the glands; the nature of this inflammation was not established definitely, but there were no indications of its being of syphilitic or tuberculous nature.

THE PATHOLOGIC ANATOMY OF FIBROUS OSTITIS. A. ABRIKOSSOFF, Russk. Klin. **5**:343, 1926.

There is reported the result of a thorough examination of a woman, aged 38, with generalized fibrous ostitis. There were extensive changes in the whole skeleton with tumor-like growths, cysts and fractures, and there was considerable enlargement of one of the parathyroid glands. The disease began with a growth in the upper jaw which was regarded as an epulis. After death the skeleton was found to be the seat of changes that varied from the early stages to the most advanced. The author reaches the following conclusions: Fibrous ostitis begins as dystrophic changes in the bone substance followed by reactive connective tissue proliferation in the marrow. He emphasizes that it is a dystrophic disease, either local or general, of bone substance, of unknown causation. The bone tissue is removed by lacunar resorption. The cysts develop from liquefaction of the connection tissue and serous accumulation; they do not represent dilated veins and lymph vessels. The size and number of cysts do not serve to differentiate between fibrous ostitis and bone sarcoma; small multilocular cysts may develop in fibrous ostitis. The giant cells in the proliferations of ostitis do not represent ostioclasts but rise from tissue developing from the endostium. The hyperplasia of the parathyroids, observed in certain cases of general fibrous ostitis, is regarded as a secondary reaction of compensatory nature as urged by Erdheim.

ARTICLES ON ATHEROSCLEROSIS. N. ANITCHKOW, W. ZINSERLING, A. SOLOWIEW, L. LOTZMANN, M. HESSE, C. WOLKOWA and A. COLEN, Arch. d. sc. biol. **25**:139, 1925.

Anitchkow writes that the arterial walls are constantly receiving diverse substances from the plasma, as the endothelium is permeable even for the

colloids of the plasma. When there is an excess of lipoids and especially of cholesterin in the blood, it tends to be deposited in the arterial walls, on the surface of the elastic fibers and in the chromotropic interstitial substance. The deposits are formed wherever the wall is exposed to mechanical influences. From this combination of local and general factors atherosclerosis arises.

Zinserling's article describes the lipoid infiltration of thrombi in the heart and aorta. This occurs in fresh as well as in organized thrombi; and, being analogous to atherosclerosis, proves that the principle lesion of atherosclerosis is primary lipoidal infiltration of the arterial walls. The opinion that atherosclerosis is a result of weakening of the walls should be abandoned.

Solowiew, in his article "Experimental Studies on the Interstitial Substance of Arterial Walls," describes the lesions produced by application of the thermocautery to the carotid artery in dogs. After the burning, the interstitial substance loses its chromotropic power, and regains it only during regeneration. From this he concludes that the chromotropic interstitial substance is a regenerative phenomenon, not regressive.

In another article, "The Accumulation of Hemosiderin in the Wall of the Aorta during Ulcerative Atherosclerosis," he finds that the direction of lymph flow is from the interior of the vessel toward the external coat. This helps to explain the development of atherosclerotic lesions of the arteries, which are due to accumulation of lipoids in the walls.

The work of Lotzmann, "The Pathologic Lesions of the Arteries of the Pelvis and Thigh," contains descriptions of the lesions found in 11 cadavers of old persons. Atherosclerosis and calcification of the middle coat were found distributed according to certain rules formulated by the author.

A similar work by Hesse is on the pathologic lesions of arteries of the arm and hand in a large number of subjects of different ages.

"Atherosclerosis of the Parrot," by Wolkowa, is a report of typical and pronounced atherosclerosis in the aorta and brachiocephalic arteries of a parrot that had been fed on a diet rich in cholesterin.

The work of Colen, "Lipoid Infiltration of the Eye," is a systematic study of accumulations of lipoids in the eyes of old persons. These accumulations form a part of analogous lesions spread throughout the organism, the principle one being atherosclerosis of the arteries.

B. R. Lovett.

Pathologic Chemistry

Plasma Protein Fractions in Normal Pregnancy. E. D. Plass and C. W. Matthew, Am. J. Obst. & Gynec. **12**:346, 1926.

During pregnancy and in the early part of the puerperium, the serum albumin is reduced while the globulin undergoes a relative but slight increase. Fibrinogen increases during pregnancy to reach the high point shortly after delivery.

Blood Serum Globulin in Leprosy. Chester N. Frazier and Hsien Wu, Am. J. Trop. Med. **5**:297, 1925.

The authors found that Sia's globulin precipitation test is positive in certain cases of leprosy, particularly in the nodular and mixed types of the disease (seventeen of thirty-two cases were positive). The percentage of blood serum globulin was increased approximately to twice the normal. Kala azar and schistosomiasis give similar globulin reactions.

E. M. Hall.

CHEMICAL ANALYSIS OF SWEAT: A FURTHER STUDY. ROBERT E. BARNEY, J. A. M. A. **87**:1827, 1926.

The sweat was obtained after injection of pilocarpine. The results suggest that senile eczema is connected with excretion of nitrogenous elements and with a diminution of chlorides in the sweat. Uric acid was not present in significant amounts in any one of twenty-nine specimens.

THE RELATIVE REACTION WITHIN LIVING MAMMALIAN TISSUES. FACTORS DETERMINING THE REACTION OF SKIN FRAFTS; A STUDY BY THE INDICATOR METHOD OF CONDITIONS WITHIN AN ISCHEMIC TISSUE. PEYTON ROUS, J. Exper. Med. **44**:815, 1926.

By means of vital staining with indicators a study has been made of the changes in reaction and in certain other attributes of a tissue abruptly rendered ischemic. Grafts of mouse skin have been employed as test material. It has been found that almost at once after implantation vigorous grafts become notably acid as compared with the normal skin and that they survive and "take" despite the acid condition, which remains at a maximum for several days. Weak or injured grafts on the contrary tend to be as alkaline as their surroundings, if not more so. Through experiments directed to the purpose reasons for this difference have been found in the lessened metabolic activities of the cells of the injured skin, and in an increased permeability which leads to a generalized suffusion of the damaged tissue with the alkaline lymph and an abnormally rapid escape of carbon dioxide from it. The influence of these factors to determine the reaction of tissues dying within the body has not been sufficiently taken into account in considering the chemical changes that occur after cell death, and some revision of current views regarding these as they affect small necrotic masses would seem called for.

Carbon dioxide penetrates so readily into the living skin as to cause some local increase in the hydrogen ion concentration within cutaneous regions exposed to an atmosphere of it, even when the local circulation and the ventilation by way of the lungs have not been interfered with. It penetrates injured skin with especially great ease.

Tissue acidosis and edema not infrequently occur together; but a relationship between them of cause and effect has not been made out.

AUTHOR'S SUMMARY.

THE RELATIVE REACTION WITHIN LIVING MAMMALIAN TISSUES. THE INFLUENCE OF CHANGES IN THE REACTION OF THE BLOOD UPON THE REACTION OF THE TISSUES. PEYTON ROUS and W. W. BEATTIE, J. Exper. Med. **44**:835, 1926.

The introduction into the blood stream of dilute hydrochloric acid or sodium carbonate in quantities not too great to be compatible with life results in marked alterations in the color of certain of the matrix tissues stainable in vivo with phenolsulphonphthalein indicators. Connective tissue in its various forms, and tendon and cartilage all become relatively more acid or alkaline than the normal. The hue of the kidney cortex also changes, as might be expected from its functions. The pancreas and lymph nodes, on the other hand, appear unaffected even when the injection is pushed to the extreme; and the slight to negligible alterations in the hue of the liver may be due to changes in the color of the associated secretion. The matrix tissues just mentioned behave as if unable to maintain a reaction of their own; whereas

the elements of the parenchymal organs would seem to make their own conditions even when so much acid or alkali has been injected as will lead to death of the animal.

Injections of lactic acid are well tolerated and it is difficult to bring about alterations in the color of the phenolsulphonphthalein stained matrix tissues by means of them. Salt solution, and sugar in large amount did not cause changes in color such as would indicate changes in reaction.

The results with the various phenolsulphonphthalein indicators are in close accord, attesting that the information these give under vital conditions is reliable.

AUTHORS' SUMMARY.

THE CHEMICAL NATURE AND SPECIFICITY OF THE MANOILOW REACTION. M. J. GALWIALO, G. E. WLADIMIROW, A. P. WINOGRADOW and W. W. OPPEL, Biochem. Ztschr. **176**:189, 1926.

THE BIOCHEMICAL BASIS OF THE MANOILOW REACTION. A. A. SCHMIDT and N. O. PEREWOSSKAJA, Biochem. Ztschr. **176**:198, 1926.

The Manoilow reaction for the determination of sex is carried out as follows: A 3 to 10 per cent emulsion of the blood is shaken, in a test tube, with 10 drops of 1 per cent papayotin, from 2 to 3 drops of 1 per cent alcoholic dahlia solution, 10 drops of 10 per cent permanganate solution, from 10 to 12 drops of hydrochloric acid and 5 drops of 2 per cent thiosinamine. A fading of the blue violet of the dye may indicate that the blood specimen is from a male.

The proteolytic ferment, papayotin, does not play any part in the reaction and may be omitted. The dye is used as an indicator. Its color persists only when the quantity of readily oxidizable protein in the blood sample exceeds the oxidizing capacity of the added permanganate. The function of the thiosinamine is the reduction and decolorization of the oxidation product, manganese dioxide.

The blood serum of females has a greater specific gravity and higher protein content than that of males, while the erythrocyte content of the whole blood is appreciably less. Since the blood specimen for the Manoilow test is diluted to a certain transparency or hemoglobin value, a preparation of blood from a female may have a greater final protein content and a correspondingly greater permanganate reduction capacity than one of blood from a male. The authors believe this to be a rather unspecific and fallible basis for a sex determination reaction.

ARTHUR LOCKE.

THE CELL AND ALBUMIN CONTENT OF THE CEREBROSPINAL FLUID IN CEREBRAL TUMOR. JENS SMITH, Deutsche Ztschr. f. d. Nervenh. **89**:278, 1926.

In 102 cases of cerebral tumor, only one third of the patients had a normal cell count, one-half had 2 or 3 cells, 25 per cent had more than 9, 15 per cent above 21 cells, and only 3 had more than 100 cells. The pleocytosis is commoner in tumor than in chronic encephalitis. There was no correlation between type or location of the tumor and the cell count. An increase in albumin content was found oftener and was greater in tumor cases than in encephalitis.

ROY GRINKER.

MICROCHEMICAL REACTIONS OF ADIPOSE TISSUE OF FETUSES AND INFANTS. G. L. DERMAN, Virchows Arch. f. path. Anat. **261**:101, 1926.

By means of microchemical reactions, Derman studied the adipose tissues of stillborn fetuses and of groups of children which had lived varying periods up to nine months. By the methods used the adipose tissue of different parts of the body was found to have a varying composition. Up to the first month of life this tissue contains a larger proportion of phosphatides and cholesterol esters, intermingled with neutral fats, than at later periods. Pathologic conditions alter the composition of the adipose tissue.

O. T. SCHULTZ.

THE CHANGES IN THE GAS METABOLISM AND THE BLOOD SUGAR CONTENT WITH ABNORMAL BLOOD REACTIONS. TADASHI ITO, Tohoku J. Exper. Med. **8**:75, 1926.

Intravenous injections of hydrochloric acid, lactic acid or monosodium-phosphate in rabbits lowered the hydrogen ion concentration, decreased the oxygen consumption and raised the blood sugar content. The blood sugar change was greater in percentage than that of the gas metabolism. The lactic acid affected the blood sugar more than the other acid solution, although the hydrochloric acid caused more effect in other ways. Intravenous injections of sodium carbonate and sodium acetate lowered hydrogen ion concentration and increased the alkaline reserve, the oxygen consumption and the blood sugar content. Blood sugar increased more after sodium carbonate, while the oxygen consumption was influenced more by the acetate. Disodiumphosphate lowered the hydrogen ion concentration yet at the same time differed from the other alkalies by lowering the carbon dioxide of the plasma, the oxygen consumption and the blood sugar content.

AUTHOR'S SUMMARY.

Microbiology and Parasitology

PULMONARY ACTINOMYCOSIS. J. C. GITTINGS and E. S. THORPE, Am. J. Dis. Child. **32**:501, 1926.

An instance of primary pulmonary actinomycosis in a child, aged 5 years, is described.

DIFFERENTIAL CHARACTERISTICS OF THE AMOEBAE OF MAN IN CULTURE. J. ST. JOHN, Am. J. Trop. Med. **6**:319, 1926.

The author attempts to differentiate the various amebas which inhabit the intestinal tract of man by means of cultural characteristics, type of movement and finer details of structure. Such a study is made possible by the large number of organisms available for observation by the culture method.

E. M. HALL.

A SIMPLIFIED METHOD FOR THE CULTIVATION OF ENDAMOEBA HISTOLYTICA. CHARLES F. CRAIG, Am. J. Trop. Med. **6**:333, 1926.

The author finds a medium consisting of Locke solution containing one part to seven of inactivated human, horse or rabbit blood serum efficient in the cultivation of *Endameba histolytica*. The best results were obtained when inactivated human blood serum was used. The excellent growth obtained demonstrates that coagulated egg or blood agar slants used as a substratum are not essential for growth, and that neither egg nor blood are essential as part of the food supply.

In this medium, *E. histolytica* has remained alive and motile for a period of eleven days, and successful transfers have been obtained in the medium after eight days. The best results in transferring cultures are obtained when these are made every twenty-four or forty-eight hours. Cultures so treated have continued active for three months without change in morphology or reproductive powers of the amebas.

E. M. Hall.

Experimentally Produced Late Bacteremia and Resolving Plague in Rats. C. L. Williams, Am. J. Trop. Med. **6**:367, 1926.

The author inoculated 2,278 wild rats (*mus norvegicus*) with plague. In a small number of these rats which showed resolving plague he was able to demonstrate the presence of a *Bacillus pestis* bacteremia. In a series of several hundred plague infected rats from 5.1 to 6.8 per cent were found to have lesions of resolving plague after twenty-one and thirty days, respectively. Nine of the first group and eleven of the second group had plague bacilli in their tissues, as demonstrated by positive results of guinea-pig inoculations. The author believes the occurrence of plague "carriers" among rats to be probable.

E. M. Hall.

The Effect of Sanocrysin on the Tubercle Bacillus after Long Exposure in Vitro. H. C. Sweany and Max Evanoff, Am. Rev. Tuberc. **14**:523, 1926.

The effect of long exposure to sodium aurothiosulphate (sanocrysin) on avirulent and virulent tubercle bacilli is recorded. A concentration of 1:2,000 does not kill all the virulent tubercle bacilli in thirty days, and in avirulent cultures, after seventy-eight days' exposure, peculiar micro-organisms were recovered that produced a "tuberculoid" condition in guinea-pigs. The micro-organisms found were motile gram-negative diplobacilli in some cases, which produced in guinea-pigs many of the characteristic changes of tuberculosis.

H. J. Corper.

The Effect of Injections of Sanocrysin on Normal and Tuberculous Dogs. Lillian Eichelberger and K. Lucille McCluskey, Am. Rev. Tuberc. **14**:533, 1926.

In tuberculous dogs, sodium aurothiosulphate (sanocrysin) is eliminated principally through the urinary tract over a period of from eighteen to thirty days. An average of 50 per cent of gold is recovered from the urine of tuberculous dogs, being 10 per cent less than that recovered from nontuberculous dogs. The urinary observations are neither consistent nor in agreement with the observations made on nontuberculous dogs. A slight febrile reaction occurred after the intravenous injection of sodium aurothiosulphate (sanocrysin) in tuberculous dogs. A high concentration of gold was found in the kidney and the liver shortly after injection, while the spleen contained a relatively small amount, and the pancreas more than the spleen. The lungs and heart contained a small but consistent amount of gold.

The Experimental Production of Abscess of the Lung. E. C. Cutler and S. A. Schlueter, Ann. Surg. **84**:256, 1926.

Attempts to produce abscess in the lung by instilling all manner of foreign and infected material into the bronchial tree have failed. The authors have succeeded in producing typical lung abscesses by introducing infected emboli

into the circulation. These emboli were prepared by filling a removed segment of vein with a blood clot bacterial culture and covering it with paraffin coated lead. If the organisms were introduced within a blood clot only, a general pneumonitis resulted. Apparently, some form of local tissue reaction must be instituted in order to lead to abscess formation. By previously operating in an infected field, that is, the intestines, a variable degree of immunity may be established, and the authors feel that abscess results when partial immunity has been produced; without immunity a general pneumonitis or lobar pneumonia results from infected clots which are set free in the circulation.

N. Enzer.

The Epidemiology of Scarlatinal Throat Infections Sine Exanthemate. Franklin A. Stevens and A. R. Dochez, J. A. M. A. **87**:2137, 1926.

The same strain of *Streptococcus scarlatinae* may cause clinical scarlet fever or scarlatina sine exanthemate. Cases of scarlatinal angina are infectious. Scarlatinal antitoxin is an efficient therapeutic agent in scarlatinal throat infections without a rash. Throat infections with *Streptococcus scarlatinae* may occur in persons who have previously had scarlet fever.

Authors' Summary.

Susceptibility of Rabbits to Infection by the Inhalation of Virulent Pneumococci. E. G. Stillman and Arnold Branch, J. Exper. Med. **44**:581, 1926.

Rabbits are very susceptible to infection by inhalation of type 1 pneumococci. When the rabbits are exposed to a pneumococcus spray the bacteria readily penetrate into the lower respiratory tract. The pneumococci which reach the periphery of the lungs as a result of this procedure usually disappear within a few hours, but frequently a generalized and fatal septicemia appears later. Pneumococci may then be recovered from the periphery of the kidney, liver and spleen. In the animals that die pleurisy and pericarditis are common, but pneumonia does not occur. Rabbits may recover from pneumococcus septicemia.

Authors' Summary.

Studies of the Bacteriophage of D'Herelle: VI. On the Virulence of the Overgrowth in the Lyzed Cultures of Bacillus Pestis Caviae (M.T.II). J. Bronfenbrenner, R. S. Muckenfuss and C. Korb, J. Exper. Med. **44**:607, 1926.

Resistants isolated from the overgrowth of cultures of *Bacillus pestis caviae* (M.T.II) lyzed by various strains of specific bacteriophage proved to be avirulent when administered to mice by feeding, or by intraperitoneal injection. These cultures remained resistant to the action of bacteriophage as long as they were carried on agar. When transferred to broth, however, one group of resistants, namely, those isolated by means of "weak" phages, became susceptible to lysis after from five to seven daily passages. The other group of resistants, isolated from one of the cultures lyzed by one of the "strong" phages, failed to become susceptible to lysis even after nearly 200 passages in broth. Simultaneous with the recovery of susceptibility, the cultures of the first group regained a degree of virulence comparable to that of the parent culture of *B. pestis caviae*. The cultures of the second group of resistants have failed thus far to recover virulence (ten months after isolation). The latter cultures, apart

from lack of both virulence and susceptibility to lysis, are identical with the parent culture of *B. pestis caviae,* as indicated by biochemical and antigenic properties. Our results offer evidence in favor of the view that resistant strains result from selection among variants already existing in the parent culture and do not arise through the inheritance of specific immunity properties produced by the action of phage.

AUTHORS' SUMMARY.

THE SURVIVAL OF TUBERCLE BACILLUS IN SUSPENSION IN PHYSIOLOGICAL SALT SOLUTION. R. E. SHOPE, J. Exper. Med. **44**:623, 1926.

Three suspensions of tubercle bacilli in physiologic salt solution were still virulent for guinea-pigs after 310, 325 and 330 days at refrigerator temperature. One of the cultures on which recent tests had been made had lost little, if any, of its virulence for guinea-pigs in 325 days.

AUTHOR'S SUMMARY.

ETIOLOGY OF OROYA FEVER: III. THE BEHAVIOR OF BARTONELLA BACILLIFORMIS IN MACACUS RHESUS. IV. THE EFFECT OF INOCULATION OF ANTHROPOID APES WITH BARTONELLA BACILLIFORMIS. V. THE EXPERIMENTAL TRANSMISSION OF BARTONELLA BACILLIFORMIS BY TICKS (DERMACENTOR ANDERSONI). HIDEYO NOGUCHI, J. Exper. Med. **44**:697, 715 and 729, 1926.

The striking fact brought out in the present study of the inoculation of *Macacus rhesus* with passage strains of *Bartonella bacilliformis* is the variety of responses which animals of the same species may manifest. The clinical features of the infection may be typical of Oroya fever or may resemble those of verruga peruviana, and in one rhesus was an instance of a type of infection in which the characteristic phenomena of both conditions were simultaneously present. Whether the appearance will resemble those of one or the other condition appears to depend on the susceptibility of the person as well as on the virulence of the organism. Moreover, it seems probable that different degrees of resistance to the invasion of the parasite on the part of the blood cells, internal organs, or skin, of the given animal may determine the predominant clinical manifestations of the infection. The factor of variation in susceptibility of different persons or different tissues of the same person would account for the variety of types of human *Bartonella* infection.

The symptoms and lesions observed in the chimpanzee and orang-utang as a result of infection with *Bartonella bacilliformis* are far milder than those of rhesus monkeys and show less resemblance to human Oroya fever or verruga.

Experiments are reported in which *Bartonella bacilliformis* was transmitted from infected to normal rhesus monkeys by the bite of a tick, *Dermacentor andersoni.* A long period of feeding, both on the infected animal and on the normal animal subjected to infection, was required in order to secure positive results. The infection transmitted by ticks was mild, but definite, as shown by the recovery of *Bartonella bacilliformis* from the lymph nodes and blood.

AUTHOR'S SUMMARY.

TISSUE DIGESTING ENZYME (HISTASE) OF STREPTOCOCCI. MARTIN FROBISHER, JR., J. Exper. Med. **44**:777, 1926.

An extracellular, proteolytic enzyme was observed in more than thirty strains of beta type, aerobic and facultative hemolytic streptococci.

The enzyme was readily demonstrable in sterile filtrates of cooked meat cultures. Gas or foul odor was not produced. It was partially inactivated by

exposure to about 60 C. for forty-five minutes or longer. The enzyme manifested itself in cooked meat cultures after about forty-eight hours' incubation at 37 C. The sterile filtrate from a ten day old culture acted within eighteen hours. From 50 to 75 per cent of the meat in a tube of cooked meat medium was digested in about three weeks at room temperature after five days' initial growth at 37 C. Correlation was not found, in the cases studied, between hemolysis and proteolysis.

Streptococci not digesting beef tissue will not digest human tissue, and those which do digest beef tissue also digest human tissue. This conclusion applies only to the nine strains studied. Ability to digest animal tissues does not necessarily imply ability to digest casein, coagulated beef serum or gelatin. The disappearance of the meat from cooked meat cultures of hemolytic streptococci was quantitatively roughly paralleled by increase of formol titrable substances in the fluid portion of the medium. The enzyme resembled trypsin in its action. Streptococci from a variety of sources, bovine, human and otherwise, showed varying degrees of proteolytic activity.

The name histase is proposed for this enzyme.

AUTHOR'S SUMMARY.

BACTERIUM PNEUMOSINTES IN CLINICAL INFLUENZA IN NEW YORK CITY IN 1926. FREDERICK L. GATES, J. Exper. Med. **44**:787, 1926.

The presence of *Bacterium pneumosintes* was demonstrated in nasopharyngeal washings from two patients in a sporadic outbreak of clinical influenza in New York in March, 1926. Two strains of bacteria morphologically similar to *Bact. pneumosintes,* but differing in certain cultural characters, and two other anaerobic filter-passing organisms were also isolated from the nine patients examined.

The blood serum of sixteen among seventeen persons convalescent from clinical influenza, and of six among ten supposedly normal persons, agglutinated one or more strains of *Bact. pneumosintes.*

AUTHOR'S SUMMARY.

STUDIES ON THE ETIOLOGY OF HEARTWATER: III. THE MULTIPLICATION OF RICKETTSIA RUMINANTIUM WITHIN THE ENDOTHELIAL CELLS OF INFECTED ANIMALS AND THEIR DISCHARGE INTO THE CIRCULATION. E. V. COWDRY, J. Exper. Med. **44**:803, 1926.

Rickettsiae of heartwater are more definitely restricted to the vascular endothelial cells of infected animals than are those of typhus or Rocky Mountain spotted fever. They likewise form more pronounced spherical colonies within the cells. Their presence does not injure the endothelial cells to a degree at all comparable with that caused by other pathogenic *Rickettsiae.* The rupture of endothelial cells and discharge of *Rickettsiae,* which are apparently viable, into the circulation constitute phenomena not thus far reported in the case of typhus or Rocky Mountain spotted fever.

AUTHOR'S SUMMARY.

A FILTERABLE VIRUS PRESENT IN THE SUBMAXILLARY GLANDS OF GUINEA-PIGS. RUFUS COLE and ANN G. KUTTNER, J. Exper. Med. **44**:855, 1926.

Certain structures in the submaxillary ducts of guinea-pigs, interpreted by Jackson as protozoan in nature, are regarded by Cole and Kuttner as probably due to the action of filterable virus. Emulsions of submaxillary glands injected into the brain and other tissues of young guinea-pigs produced symptoms and changes indicating the presence of an infective agent which was not held back

by Berkfeld N filter impermeable to bacteria. The work presents additional evidence that nuclear inclusions in cells indicate the action of agents of the group of filterable viruses.

AUTHORS' SUMMARY.

INVOLUTION FORMS OF ESCHERICHIA COLI. A. T. HENRICI, J. Infect. Dis. **39**:429, 1926.

Measures of the rate of death and of autolysis, and of variation in form of bacteria are described and discussed. The rate of autolysis may be estimated by the time intervals, between the curves for death of the cells as determined by plate counts, and as determined by their staining with Congo red. The degree of variation in form has been computed by the products of the frequency of the various cell types and the reciprocal of their mean frequency, the fluctuations being expressed as index numbers.

The rate of death and autolysis, and the degree of variation in form have been determined in five cultures of *Escherichia coli* grown on peptone agar; acid, neutral and alkaline in reaction, and containing sodium chloride and calcium chloride, respectively.

Correlation could not be established between the degree of variation in form and the rate of death or the favorableness of the medium for growth.

There was found a definite rank order correlation between the degree of variation in form of the cells and the rate of autolysis of the dead cells. The rate of autolysis in the various cultures was as follows: alkaline, 17 days; neutral, 13.25; salt, 6.25; acid, 4.25; calcium chloride, 4. The mean index of variation in form of the cells was as follows: alkaline, 67.71; neutral, 87.56; sodium chloride, 93.01; acid, 93.42; calcium chloride, 157.25.

AUTHOR'S SUMMARY.

STUDIES ON EXPERIMENTAL ENCEPHALITIS. EARL B. MCKINLEY and MARGARET HOLDEN, J. Infect. Dis. **39**:441, 1926.

Two strains of herpes virus (one Levaditi virus) have been found to become attenuated when dilutions are made in physiologic salt solution or in fresh rabbit serum and kept at icebox temperature or incubator temperature from three to thirty days.

Rabbits can be highly immunized against the herpes virus by repeated subcutaneous injections of normal rabbit serum, virus mixtures prepared from infected brains. The animals become immune to concentrated doses of fresh virus administered subdurally.

The serums from such hyperimmunized animals may exhibit marked virucidal properties and completely neutralize the fresh virus when left in contact with it for as short a time as three days at icebox temperature.

Attempts to culture the virus on Noguchi's medium at various reactions at different temperatures, under aerobic and anaerobic conditions have failed.

Cross immunity experiments with the LeFevre herpes virus and the Levaditi so-called encephalitis virus have been positive, confirming the work of others in establishing the biologic identity between these two viruses.

The herpes virus is markedly susceptible to the action of ultraviolet rays as generated by the Alpine sun lamp. Exposures of supernatants from concentrated brain emulsions in salt solution for only five minutes destroy the virus. Test animals surviving subdural injections of rayed virus are found not to possess immunity when subsequent injections are given with the fresh virus.

Vesicular fluids obtained from cases of herpes zoster when injected subdurally into rabbits have given negative results.

AUTHORS' SUMMARY.

THE NATURE OF BACTERIOPHAGE. EARL B. MCKINLEY and MARGARET HOLDEN, J. Infect. Dis. **39**:451, 1926.

We concur with d'Herelle that the bacteriophage is a particulate substance. Being particulate does not in and of itself imply its living nature though its power of multiplication and adaptation are strong arguments for it. We question the theory of its being an ultramiscropic virus, in that adequate proof is lacking for this conception. However, it is possible to conceive of an ultramicroscopic particulate substance, diastatic in its action, granular in form and inanimate, which may be derived from the bacterial cell during a stage in its life cycle as a result of the influence of tissue cells of the host have had on it. Bordet has called this "hereditary vitiation" and it may well be. The susceptibility of the bacteriophage to the action of ultraviolet rays is suggestive of its living nature though it is well known that enzymes are also destroyed by them and such a criterion would not serve in proving this point.

AUTHORS' SUMMARY.

DISTRIBUTION OF SPORES OF BACILLUS BOTULINUS AND BACILLUS TETANI IN THE SOIL: 1. IN MARYLAND. S. R. DAMON and L. B. PAYABAL, J. Infect. Dis. **39**:49, 1926.

Five samples did not contain any toxin producing organisms demonstrable by the methods used. Four contained toxin producing organisms that could not be identified by antitoxin protection tests. *Bacillus tetani* was present alone in 6 samples. *Bacillus botulinus*, type A, was present alone in 8; *Bacillus botulinus*, type B, was present alone in 25, and *Bacillus botulinus*, type C, was present alone in 5 samples. *Bacillus botulinus*, types A and C, were present together in 4, and *Bacillus botulinus*, types B and C, were present together in 5 samples. The three types of *B. botulinus* were not found together, and nor were *Bacillus botulinus* and *Bacillus tetani* found together in any single sample.

AUTHORS' SUMMARY.

EFFECT OF THE CALCIUM, VITAMIN C, VITAMIN D RATIO IN DIET ON THE PERMEABILITY OF INTESTINAL WALL TO BACTERIA. AGNES H. GRANT, J. Infect. Dis. **39**:502, 1926.

An adequate balance between dietary calcium, vitamin C and vitamin D is essential in maintaining the normal resistance of the intestines to the migration of intestinal bacteria into the blood stream.

A severe disturbance in the proper ratio between vitamin C and vitamin D increases the permeability of the intestines to bacteria. This is true when there is both an excess of vitamin D and a deficiency of vitamin C, and when there is an excess of vitamin C and a deficiency of vitamin D.

The oxidation of cod liver oil destroys its content of vitamin A, but it does not destroy the factor that is responsible for the marked decrease in intestinal resistance.

Oxidizing the orange juice destroys its power to inhibit the factor in cod liver oil that is responsible for the marked decrease in intestinal resistance due to the cod liver oil factor.

An excess of calcium seems to favor the migration of bacteria into the blood stream whenever used; and when vitamin C and vitamin D are both deficient, it seems to favor a rapid multiplication of the bacteria in the spleen and lungs.

AUTHOR'S SUMMARY.

EPIDEMIC LYMPHADENITIS WITH FORMATION OF ABSCESS IN GUINEA-PIGS DUE TO INFECTION WITH HEMOLYTIC STREPTOCOCCUS. J. G. HARDENBERGH, J. Lab. & Clin. Med. **12**:119, 1926.

An epidemic disease in guinea-pigs which is characterized by lymphadenitis with the formation of abscesses in the superficial lymph nodes is described. The cause of the disease is a hemolytic streptococcus of the pyogenes group. The natural infection is chronic and comparatively inocuous; artificial infection is usually acute and rapidly fatal. The disease presents a seasonal variation and occurs more frequently in females than in males. The source and mode of the natural infection are not established.

S. A. LEVINSON.

STRONGYLOIDES INTESTINALIS INFECTION. M. P. NEAL and H. P. MUIR, J. Missouri M. A. **23**:369, 1926.

A case of strongyloides intestinalis infection from Missouri is described. Probably the infection was acquired from association with Chinese students.

CONTRIBUTION TO THE QUESTION OF DYSENTERY CARRIERS IN THE PHILIPPINE ISLANDS. ANA VAZQUES-COLET, Philippine J. Sc. **28**:173, 1925.

The existence of healthy carriers of *B. dysenteriae* in the Philippine Islands has been demonstrated.

The proof was carried out by isolation of cultures which, according to standard methods of identification, proved to be *B. dysenteriae*.

In 3,328 examinations, fourteen carriers were found, of whom seven harbored the Shiga type, six the Flexner type, and one both Flexner and Shiga types successively.

Agglutination tests were performed with the carriers' serums and with the corresponding culture isolated from the carriers, as well as with stock cultures of the Shiga and the Flexner types. Usually the serum of the carrier agglutinated its own strain to a lesser degree than the stock cultures, and at times a considerable inhibition zone was noticed with the carrier's serum and its own strain.

All of the cultures belonging to the Shiga type isolated from the carriers were pathogenic for white mice, and some of them were strongly toxic to rabbits. The cultures belonging to the Flexner type, isolated from carriers, were found to be of low virulence.

FURTHER STUDIES ON STREPTOCOCCI FROM SCARLATINA, ERYSIPELAS AND PUERPERAL FEVER. G. H. EAGLES, Brit. J. Exper. Path. **7**:286, 1926.

All strains of hemolytic streptococci from scarlet fever produce toxic filtrates as judged by intracutaneous tests. A large number of strains from erysipelas, puerperal fever and various other pathologic conditions produce a similar toxic filtrate. All toxic filtrates, regardless of their source, are neutralized by scarlet fever horse serum. Results obtained when immune rabbit serums from various toxin-producing strains are used for neutralization may indicate, however, higher specificity. By agglutination three main groups are shown to exist

among hemolytic streptococci. The scarlet fever and erysipelas groups are confirmed and a similar grouping is shown among strains from puerperal fever. Toxin production and agglutination by scarlet fever immune serums are not closely related when strains from a variety of pathologic sources are studied.

S. A. Levinson.

Experimental Pneumococcal Infections of the Lung. J. F. Gaskell, J. Path. & Bacteriol. **28**:427, 1925.

Experiments were conducted on rabbits in an endeavor to throw light on the pathogenesis of the various forms of pneumococcal infection of the lung. The infecting dose in 1 c.c. of fluid was introduced into a lobe of the lung by insufflation through a tracheotomy opening by means of a soft rubber catheter. A single strain of pneumococcus of known virulence was used. The author obtained infections of the lung differing greatly in distribution and constitutional effect, but closely comparable with the various lesions in man. He found that the type of lesion depends on the virulence of the organism introduced and not on the dose given. With cultures of low virulence (titer 3:4) bronchopneumonia of the central and root areas resulted, which remained localized. With a titer between 4 and 5, the bronchopneumonic lesions are more widespread, coalescing to give a lobular pneumonia of the posterior part of the lung. With a titer of 5 to 6, the whole lobe of the lung is involved, and pleurisy and pericarditis frequently result. A titer of 6 or more produces an intense septicemia with miliary lesions in all lobes of the lung. The milder infections are more catarrhal, while the more virulent ones are characterized by a marked exudation of polymorphonuclear leukocytes.

E. M. Hall.

The Preparation of Certain Substituted Ureas and Their Use in the Treatment of Trypanosomiasis. T. H. Fairbrother, F. A. Mason, W. H. Perkin, Arnold Renshaw, J. Path. & Bacteriol. **28**:515, 1925.

Mice inoculated with heavy doses of *Trypanosoma equiperdum* were treated with three different substituted ureas. One of these (No. 3) gave evidence of definite trypanocidal properties. This urea has the formula suggested by Fourneau. The tolerated dose is 10 mg. per 20 gm. mouse, the curative dose was as low as 0.05 mg., a C/T ratio of 200/1.

E. M. Hall.

The Histology of the Primary Pulmonary Focus in Tuberculosis in the Guinea-Pig. W. Pagel, Beitr. z. klin. Tuberk. **61**:678, 1925.

The primary pulmonary focus in man and guinea-pig are alike in the marked tendency to reparation and to the formation of a capsule of connective tissue around an exudative center and in regard to the caseous process in the regional lymph glands. These characteristics make it possible to distinguish the primary lesion in the guinea-pig from later foci.

Max Pinner.

Pyocyaneus Infection in Infants. Hermann Chiari, Centralbl. f. allg. Pathol. u. path. Anat. **38**:483, 1926.

In autopsies on three children, all about a week old and dying presumably from "Toxic Grippe and Erythema," a meningitis and pericarditis were found due to *Bacillus pyocyaneus*. Cultures of the organism from the brain and bowel killed guinea-pigs in twelve hours and produced pyocyanase abundantly. The

exudate on the brain was thickest in the frontal region and consisted of an outer layer rich in pus cells and extracellular bacilli and an inner cell-poor layer rich in fibrin. In contradiction of Fraenkel's reports the exudate was never hemorrhagic and bacilli were not found in the arterial walls. In one instance microscopic hemorrhages were found at the junction of cortex and medulla in the brain, and in another bronchopneumonic foci were found in the lungs.

GEORGE RUKSTINAT.

THE BACTERICIDAL ACTION OF HYDROCHLORIC ACID-FREE GASTRIC JUICE. W. LÖWENBERG, Klin. Wchnschr. **5**:1868, 1926.

In a majority of the patients examined the gastric secretion has a distinct bactericidal action independent of its hydrochloric acid content. In neutral and alkaline gastric juices this action is directly effective; in acid juices after neutralizaton.

J. D. WILLEMS.

THE GUARNIERI BODIES. VICTOR SCHÜTZ, Ztschr. f. Hyg. u. Infectionskrankh. **105**:1, 1925.

Schütz examined histologically the corneas of rabbits which had been inoculated with vaccine and with material from smallpox. He concludes that the Guarnieri bodies are derived from the cytoplasm and formed in response to infection or poisoning of the cells. Nothing suggests the presence of the virus of smallpox in the Guarnieri bodies.

W. OPHÜLS.

THE D'HERELLE PHENOMENON. III. RELATION OF BACTERIOPHAGE TO AGGLUTINATION. KURT MARCUSE, Ztschr. f. Hyg. u. Infectionskrankh. **105**:17, 1925.

Investigation of the effect of the corresponding bacteriophage and immune serum on a Y strain which is highly sensitive to bacteriophage reveals a connection between the sensitivity to bacteriophage and the agglutinability and the absorption of agglutinin. This suggests that the point of attack on the surface of bacteria is the same for bacteriophage and for agglutinin. Loss of sensitivity to bacteriophage is associated with decrease of the power to bind agglutinin. Blocking of the "agglutinogen" decreases the sensitivity to bacteriophage.

W. OPHÜLS.

THE EFFECT OF HYDROGEN ION CONCENTRATION IN THE DEVELOPMENT OF SO-CALLED LEPRA BACILLI ON NUTRIENT MEDIUMS. SEIGO KONDO and RISHICHI NODAKE, Ztschr. f. Hyg. u. Infectionskrankh. **105**:67, 1925.

The limits of growth of several acid-fast bacilli obtained from leprous material on nutrient mediums of different p_H were found to be quite wide like those of saprophytic acid-fast bacilli.

W. OPHÜLS.

CHEMISTRY OF BACTERIAL TOXINS. C. HALLAUER, Ztschr. f. Hyg. u. Infectionskrankh. **105**:138, 1925.

Aqueous solutions of dysentery and of diphtheria toxin lose their toxicity on the addition of acid. This reaction is reversible. The toxin is reactivated by the addition of a proper amount of alkali. It is suggested that this phenomenon is due to an intramolecular rearrangement of the toxin molecule in such a way that by the addition of acid certain closed rings in the molecule are

transformed into open chains which resume their cyclic arrangement on the addition of alkali. It is hoped thatthis reaction may be a means of obtaining more precise information in regard to the chemical structure of the toxins.

W. Ophüls.

The Nature of the Bacteriophage. H. Munter and K. Rasch, Ztschr. f. Hyg. u. Infectionskrankh. **105**:204, 1925.

Changes in resistance to the bacteriophage occur only in cultures which spontaneously produce bacteriophage. They cannot be used as a conclusive proof of the living nature of the bacteriophage.

W. Ophüls.

Susceptibility of Young and Old Mice to Recurrent Fever. A. Feldt and A. Schott, Ztschr. f. Hyg. u. Infectionskrankh. **105**:241, 1925.

Ninety-five per cent. of adult mice become infected following feeding of blood containing a considerable number of the spirochetes of recurrent fever. Of suckling mice, only 24 per cent. become infected, and the infection was never severe.

W. Ophüls.

Poisoning in Man by Ingestion of Meat of Hogs Intravitally Infected with Paratyphoid Bacillus and Bacillus Enteridis. Max Müller, Ztschr. f. Hyg. u. Infektionskrankh. **106**:468, 1926.

On the basis of his own experience and that of others, the author comes to the conclusion that the intravital infection of hogs with paratyphoid bacilli can be transmitted to man by the consumption of the meat of the infected animals. He believes that this occurs more frequently than is now recognized. According to Müller a part of the infections with paratyphoid bacilli arising from the use of sausages or chopped meat are due to the presence in these food stuffs of the meat of hogs that had been suffering from a latent paratyphoid infection. These latent infections cannot be recognized by gross inspection of the slaughtered animals. The relatively few bacteria which are present in the tissues during life multiply greatly after death when conditions are favorable. The consumption of infected meat products of this kind, raw or imperfectly sterilized, causes large outbreaks of paratyphoid infection in man. All types, the Gärtner bacillus, the paratyphoid bacillus beta and the Voldagsen types, are pathogenic both to animals and to human beings.

W. Ophüls.

The Relation of Herpetic Infection to Encephalitis. S. Dmitrieff, Ztschr. f. Hyg. u. Infektionskrankh. **106**:547, 1926.

Dmitrieff noticed the interesting fact that the virulence of the herpetic virus is greatly decreased by passage through the brain of guinea-pigs.

W. Ophüls.

Experimental Recurrent Infection of Rabbits. R. Prigge, Ztschr. f. Hyg. u. Infektionskrankh. **106**:552, 1926.

Prigge observed that a certain strain of African recurrens spirilla caused a serious infection when large doses of mice blood containing numerous spirochetes were injected intravenously in rabbits. The infection could be transmitted from rabbit to rabbit but only to a limited degree on account of a progressive loss of virulence. By intracutaneous inoculation he succeeded in

producing in rabbits a purely local lesion, a recurrens chancre, in which the presence of living spirochetes could be demonstrated for about two weeks.

W. Ophüls.

The Significance of Pathologic Changes in the Lymph Nodes in the Venous Angles in Tuberculosis. A. Ghon, H. Kudlich and St. Schmiedl, Ztschr. f. Tuberk. **46**:197, 1926.

The term exogenous reinfection should be applied only when an infection takes place from the outside after the first infection is biologically healed; if it occurs before healing is complete, it should be termed superinfection. Many cases of so-called endogenous reinfection are really exacerbations of a still active lesion. Ghon introduced the term "Lymphoglandular endogenous reinfection" for cases in which recent tuberculous lesions are found in the area of lymph drainage of the glandular lesion of an apparently healed primary complex. Such observations demonstrate the possibility of a slow and unnoticed extension from the primary complex, possibly into the blood stream, causing a hematogenous phthisis. One hundred persons with various tuberculous foci were examined in regard to lesions extending from the primary complex into the lymph nodes of the venous angles. In 95 per cent a pulmonary primary infection was demonstrable. In 84 per cent of the cases definite tuberculous lesions were found in these nodes, and in an additional 4 per cent changes which were suggestive of tuberculosis. These lesions were of various ages; epitheloid cell tubercles were found as well as hyalinized and partly calcified foci. Since such changes were found, both in tertiary phthisis and in cases which did not show any other lesions but an apparently healed pulmonary primary focus, a hematogenous reinfection may develop without the passage of the virus through the arterial circulation.

Max Pinner.

Research on the Bacteriophage. L. K. Wolff, Nederlansch Tijdschr. v. Geneesk. **2**:1215, 1925.

Trypsin loses its bacteriophage-like action when diluted to 1:200, while bacteriophage is still active at this dilution, even after adsorption by kaolin. It is suggested that the action of trypsin is due to the presence of bacteriophage in the trypsin. This has been d'Herelle's contention, while others have hailed this action of trypsin as evidence that the bacteriophage is of the nature of ferment.

Immunology

Fatal Asthma. Report of a Case with Autopsy. Francis M. Rackemann, Boston M. & S. J. **194**:531, 1926.

A well nourished woman, aged 43, with a history of hay-fever between the ages of 14 and 31, and positive skin reactions to timothy and ragweed, when the hay-fever stopped began to have attacks of asthma, at long intervals. Two years ago, however, this asthma became very much aggravated, and the attacks came more often and were of longer duration. Finally, death occurred during a severe paroxysm.

In spite of positive skin reactions, the evidence of an extrinsic cause of her asthma was not clear, since attacks had occurred at different seasons and with different surroundings. Removal to a room in the hospital relatively free from dust did not help her. The fact that the asthma occurred in well defined attacks, is unexplained.

Clinically, there was no cause of death other than asthma, and at necropsy there was only acute dilatation of the right ventricle, together with pulmonary emphysema. No changes were observed in the musculature of the bronchi.

There are only a few cases reported in the literature in which death can be attributed with certainty to uncomplicated bronchial spasm; most of these cases are found in the article on the pathology of bronchial asthma by Huber and Koessler (*Arch. Int. Med.* **30**:689, 1922).

THE KAHN TEST. J. E. HOUGHTON, O. B. HUNTER and TOMAS CAJIGAS, J. A. M. A. **87**:1898, 1926.

The Kahn test is praised as simple and easily carried out everywhere; it is more sensitive than the Wassermann test in treated patients and in the primary stage.

THE BEHAVIOR IN VIVO OF CERTAIN RELATIVELY PURE ANTIGENS. F. S. JONES, J. Exper. Med. **44**:625, 1926.

Precipitin tests of the blood serum and the urine of rabbits which had received injections of crystallized egg albumin (intravenously) or casein (intraperitoneally) were made with the rabbit antiserums for the respective antigens. It became evident, then, that the reaction of a rabbit to a single injecion of a relatively pure protein will depend on the character of the protein injected. When crystallized egg albumin is administered it is rapidly eliminated from the circulation. The rapid disappearance of the egg albumin from the blood stream is partly accounted for by its prompt elimination through the urine. Antibody appears in the serum from the seventh to the tenth day. Casein behaves differently. It persists in the blood for a considerable period; after the seventh or eighth day both antigen and antibody may be demonstrated in the blood. Casein cannot be detected in the urine following its injection into the body. The behavior of casein in the body affords an analogy with the conditions frequently noted after the administration of foreign serum, in both cases both antigen and antibody may be present in the circulation together.

AUTHOR'S SUMMARY.

IMMUNOLOGICAL RELATIONSHIPS OF ENCAPSULATED AND CAPSULE-FREE STRAINS OF ENCAPSULATUS PNEUMONIAE (FRIEDLÄNDER'S BACILLUS). L. A. JULIANELLE, J. Exper. Med. **44**:683, 1926.

"S" strains of Friedländer's bacillus produce capsules and soluble specific substance, and are of exalted virulence. "S" strains are type specific and react with only the type specific antibodies of the homologous types. Immunization with "S" cells induces the formation of antibodies which agglutinate type-specifically, precipitate the corresponding soluble specific substance, and protect white mice against infection caused by organisms of the same type.

"R" strains of Friedländer's bacillus do not produce capsules or soluble specific substance, and are not pathogenic. "R" strains are serologically undifferentiated from each other and react only with the specific antibodies. Immunization with "R" cells induces antibodies which do not agglutinate encapsulated organisms, do not precipitate soluble specific substances and do not afford protection against infection by Friedländer's bacillus. Anti-R serum contains only the species antibody which reacts with any capsule-free organism regardless of its type origin.

Decapsulation of "S" cells by heat and acid chemically converts a type reacting organism into a species reacting organism.

AUTHOR'S SUMMARY.

IMMUNOLOGICAL RELATIONSHIPS OF CELL CONSTITUENTS OF ENCAPSULATUS PNEUMONIAE (FRIEDLÄNDERS BACILLUS). LOUIS A. JULIANELLE, J. Exper. Med. **44**:735, 1926.

The soluble specific substance of Friedländer's bacillus is nonantigenic when dissociated from the cell. It is different for each type and it is highly reactive in the corresponding anti-S serum.

The nucleoprotein is antigenic, induces the species or protein antibody which reacts with capsule-free cells and protein derived from all types. Antiprotein serums do not react with either the encapsulated cell or the polysaccharide derived from it, and they do not offer protection against infection.

Anti-R and antiprotein serums are identical in their behavior.

The carbohydrate of Friedländer's bacillus is demonstrable in filtrates of actively growing cultures and in the blood and urine of infected animals.

The protein is demonstrable in filtrates of only old, disintegrating cultures.

AUTHOR'S SUMMARY.

AN EXPERIMENTAL ANALYSIS OF BACTERIAL ALLERGY. HANS ZINSSER and TAKEO TAMIYA, J. Exper. Med. **44**:753, 1926.

A nitrogenous, probably protein, constituent of the bacterial growth or of its body substance stimulates a specific reaction in the tissue cell by which its specific capacity to establish contact with this constituent is enhanced. The cell is thereby enabled to exert an effect, probably enzyme-like, on this material, in consequence of which a toxic substance is liberated, largely on or possibly within the cell itself.

Both processes may be dependent on one and the same reaction body. But it seems more likely that increased contact and the increased cell activity are separately developed, an assumption which is rendered probable by the association of the highest degrees of allergy with inflammatory cell reactions, and by the fact that moderate and less specific allergic sensitiveness follows ten or more days after the administration of considerable amounts of indifferent protein substances to guinea-pigs. We interpret this as signifying that such injections may nonspecifically increase cellular activity, a change which many earlier workers have spoken of as "cell irritability."

Both processes are closely associated with the altered cell itself, and the factors by which the reaction is brought about are not easily given up to the blood steam as are the antibodies formed in response to injections of proteins or whole bacteria.

One is confronted, therefore, with an immunologic mechanism which has some close analogies to those others in which circulating antibodies are formed, but which differs from these mainly in the intimacy with which the entire reacting system is associated with the cells themselves. It is difficult to conceive that a functional cell alteration, as profound as this, should be entirely unrelated to the phenomena of susceptibility or resistance.

AUTHORS' SUMMARY.

THE INDIVIDUALITY OF SEMEN [HUMAN] WITH REFERENCE TO ITS PROPERTY OF INHIBITING SPECIFICALLY ISOHEMOAGGLUTINATION. K. YAMAKAMI, J. Immunol. **12**:185, 1926.

Human semen has the power to absorb or neutralize human iso-agglutinins. If semen and serum are mixed in the proper proportions, the semen will suspend the action of the iso-agglutinin in the serum in the same specific manner as do

the corpuscles of the person from whom the semen was obtained. In other words human semen contains the same iso-agglutinable group elements as the blood of the man in question. Yamakami states that saliva and vaginal secretion also contain such elements. As the inhibiting substance is stable and can be extracted from seminal stains older than 4 months, it is suggested that it can be used for practical purposes in attempts to trace seminal stains to a single man.

STUDIES IN HYPERSENSITIVENESS [SENSITIVENESS OF ASTHMATICS]. A. H. FINEMAN, J. Immunol. **12**:191, 1926.

By the intradermal or scratch method, asthmatic patients sensitive to rabbit hair, horse dander or cottonseed can be classified according to degree of skin sensitiveness. By preliminary tests it is possible to reduce the constitutional reactions following intradermal diagnostic tests or specific treatment.

STUDY OF POLLEN IMMUNE SERUM. SUSAN GRIFFITH RAMSDELL, J. Immunol. **12**:231, 1926.

Small animals injected with pollens may give positive fixation precipitin, cutaneous and anaphylactic tests; passive sensitization is demonstrable by the Schultz-Dale method. These reactions are not strictly specific. Pollens contain in common a muscle stimulating substance.

GROUP SPECIFIC SUBSTANCES IN HUMAN SPERMATOZOA. K. LANDSTEINER and PHILIP LEVINE, J. Immunol. **12**:415, 1926.

Small amounts of spermatozoa absorb specifically the group agglutinins of immune rabbit serum, thus establishing that human spermatozoa contain substances which are identical or similar to the iso-agglutinable factors A and B of human corpuscles.

HEPARIN INHIBITION OF ANAPHYLACTIC SHOCK. PRESTON KYES and E. R. STRAUSER, J. Immunol. **12**:419, 1926.

In pigeons the intravenous injection of 1 cc. of a 1 per cent solution of heparin forty-five minutes before the injection of the second or critical dose of sheep serum practically eliminates all symptoms of anaphylactic shock. As heparin inhibits fibrin formation, it is suggested that there is "a causal relation between fibrin emboli and the symptoms of shock."

THE ISOLATION OF SUBSTANCES WITH IMMUNE PROPERTIES. ARTHUR LOCKE and EDNA RUTH MAIN, J. Infect. Dis. **39**:484, 1926.

Highly purified preparations of diphtheria antitoxin may be secured by isoelectric fractionation of the Ramo toxin-antitoxin precipitate. These preparations contain from 0.0005 to 0.0015 mg. of nitrogen per antitoxic unit; have the anaphylactogenic character of horse serum protein, and do not withstand boiling. The avidity and therapeutic usefulness of antitoxin preparations are diminished by aging and heating.

AUTHORS' SUMMARY.

EFFECT OF TREATMENT ON THE WASSERMANN REACTIONS OF SYPHILITIC PATIENTS. ERNEST GLYNN, R. E. ROBERTS and PHOEBE U. RIGLAND, Medical Research Council, Special Report Series, No. 107, 1926.

Mercurial treatment in Wassermann-negative or "latent" syphilis increases rather than diminishes the tendency to clinical or Wassermann relapses.

THE ACTION OF SENSITIZED ANTIGEN IN THE PRODUCTION OF SPECIFIC AND ISOPHILE HEMOLYTIC IMMUNE BODY. TSUNENORI IIJIMA, J. Path. & Bacteriol. **28**:397, 1925.

Iijima presents data tending to prove that the sensitization of antigen leads to a neutralization of antigenic power, since the amount of immune body produced as the result of injecting fully sensitized antigen into animals is in general infinitesimally small as compared with that in control tests.

Rabbits receiving injections with ox corpuscles that had been saturated with immune body or with sensitized guinea-pig kidney cells produce only a small amount of specific immune body. Goat corpuscles sensitized with the Forrsman antibody and guinea-pigs receiving injections with goat corpuscles that have been sensitized with isophile antibody produce only a small amount of isophile hemolysin.

E. M. HALL.

THE NATURE OF THE ACQUIRED RESISTANCE TO BACTERIOPHAGE ACTION. F. M. BURNET, J. Path. & Bacteriol. **28**:407, 1925.

Burnet worked with three types of bacteriophage obtained from the urine or feces of patients. One patient was suffering from chronic pyelitis, the other two from typhoid fever. The results are interpreted in the light of Seiffert's "catalyst" theory of acteriophage activity but modified to bring the phenomena of bacterial fission and of transmissible lysis into close interdependence. The data tend to show that resistance acquired by a small proportion of sensitive bacilli in the presence of appropriate bacteriophage depends on some variable factor in the bacilli rather than on variations in the bacteriophage. Bacilli that have acquired resistance to one phage may become sensitive to one or more phage types toward which they were previously resistant. Long filamentous forms of the coliform organisms studied in which growth occurs without normal fission are considered an early stage in the development of resistance.

E. M. HALL

THE CONDITIONS GOVERNING THE APPEARANCE OF TÂCHES VIÈRGES IN BACTERIOPHAGE ACTIVITY. F. M. BURNET, J. Path. & Bacteriol. **28**:419, 1925.

The experiments deal with the relationship between the number of bacilli and the number of phage particles in the production of tâches vièrges. The author found that when different dilutions of phage were plated with constant heavy inoculations of bacilli, the number of plaques was proportional to the amount of phage added. The number of plaques obtained from a given quantity of phage, however, was dependent to a great degree on the number of bacilli present. He believes that the fundamental differences in the activities of phages depends on the directness with which they are adsorbed to the bacilli. Any bacillus in which direct adsorption of lytic particle occurs becomes a center for lysis. With an active phage such adsorption is rapid and direct, while with less active ones the lytic particle is weakened by the associated inert bacterial protein, and both adsorption and stimulation are slower.

E. M. HALL.

A CONTRIBUTION TO THE STUDY OF IMMUNITY IN INVERTEBRATES. S. METALNIKOV, Ann. de l'Inst. Pasteur **40**:787, 1926.

The author conceives of two distinct types of immunity, lack of susceptibility of the living cell to toxin or poison, and the immunity of defense, based on an increased sensitivity of the cell, manifested by the faculty of the cells to

react in combating bacteria and parasites entering the body. In the lower animals the first form of immunity predominates, while in the vertebrates a cellular active immunity is more important. Humoral antibodies are a secondary phenomenon found chiefly in the higher animals. In insects the author was never able to demonstrate agglutinins, precipitins, opsonins, amboceptor or compliment. Occasionally, bacteriolysin was found.

G. B. RHODES.

DERMATOSIS DUE TO ASCARIDIASIS, RESEMBLING HEBRAS PRURIGO. A. CEDERBERG, Arch. f. Dermat. u. Syph. **150**:393, 1926.

The case of a boy, aged 8 years, physically retarded, with many ascaris eggs in the stool and the skin dry and pigmented in places, was diagnosed as Hebra's prurigo. From the age of 6 months to 5 years he had had a generalized, itching, pin-head sized, papular skin eruption which was then supplanted by a small papular rash most marked on the extensor surfaces but noticeable also on the flexor surfaces, abdomen and back. After the administration of santonin, fifty-seven ascarids were passed. The author concludes that ascari infection may lead to urticaria, an anaphylactic manifestation of an intoxication. At the height of the intoxication there were 15,500 lymphocytes per cubic millimeter, and the eosinophils constituted 47 per cent of the white cells. The hemoglobin was 70 per cent (Sahli) and the red cell count was between 3,500,000 and 4,000,000.

GEORGE RUKSTINAT.

THE PRODUCTION OF LOCAL TUBERCULIN ALLERGY IN GUINEA-PIGS AND MAN: II. EXPERIMENTS WITH LANGER'S VACCINE NO. 147. H. FERNBACH, Beitr. z. klin. d. Tuberk. **64**:387, 1926.

A large percentage of guinea-pigs treated intraperitoneally with this vaccine developed a specific skin sensitiveness to tuberculin. Children who received subcutaneous injections showed small nodules and scars at the site of injection and some swelling of the regional lymph glands. They too developed slowly a skin allergy against tuberculin.

MAX PINNER.

EXPERIMENTS CONCERNING THE TUBERCULIN REACTION. P. KIMMELSTIEL, Beitr. z. klin. Tuberk. **64**:422, 1926.

Old tuberculin on which *Bacillus cytolyticus* Much was cultivated for eight days did not produce any skin reaction in allergic persons. If, however, certain lipoids were added to this modified tuberculin it caused reactions again in persons with active tuberculosis but not in healthy allergic persons. In a second series of experiments it was found that the activating potency of lipoids was increased by the addition of proteins and that it was decreased by the addition of protein split products.

MAX PINNER.

THE TUBERCUMET REACTION. F. BAUM and L. P. BLACK, Beitr. z. klin. Tuberk. **64**:429, 1926.

Tubercumet (Lilly & Co.) was tested on eighty-four patients and on eighty-two animals. Positive reactions were obtained in nontuberculous animals. Of fifty-four tuberculous patients thirty-two reacted negatively. The authors consider the reaction as nonspecific and not helpful in the diagnosis of tuberculosis.

MAX PINNER.

THE RELATION BETWEEN BLOOD-GROUPS AND TUBERCULOSIS. M. M. ALPERIN, Beitr. z. klin. Tuberk. **64**:500, 1926.

One hundred and forty-seven Russian and Jewish patients with tuberculosis were grouped (Moss). Tuberculosis was found more frequently in the second and to lesser extent in the fourth group. A particular tendency to frequent and copious hemoptisis was noticed in persons belonging to the first and fourth groups.

MAX PINNER.

IS THE DISTRIBUTION OF THE BLOOD GROUPS DIFFERENT IN PATIENTS WITH PULMONARY TUBERCULOSIS FROM THAT IN HEALTHY PERSONS? J. HOLLÓ and W. LÉNARD, Beitr. z. klin. Tuberk. **64**:513, 1926.

Two hundred patients with pulmonary tuberculosis and an equal number of healthy persons were examined. A marked difference in the distribution of the blood groups was not noted.

MAX PINNER.

THE ORIGIN OF SYPHILITIC BLOOD CHANGES AND THE CHARACTERISTICS OF AN ANTISPIROCHETAL SERUM. FELIX KOPSTOCK, Deutsche med. Wchnschr. **52**: 1460, 1926.

Injected in rabbits, killed spirochetes induced rapid and abundant formation of antispirochetal substances as well as antibodies for organ lipoids. The serum of rabbits so treated contain agglutinins and fix complement in high dilution.

THE ABDERHALDEN PRINCIPLE AND ITS DEMONSTRATION BY A PRECIPITIN REACTION. H. LOESCHCKE and H. LEHMANN-FACIUS, Klin. Wchnschr. **5**:1924, 1926.

Extracts of the kidney, liver and heart of rabbits are injected intraperitoneally into rabbits. When twelve days later the rabbit serum is mixed in equal parts with the specific antigen a flocculation takes place. The ninhydrin test on the mixture is invariably positive. This mixture consists of two unequal molecules formed as protein decomposition products, the larger of which is precipitated by alcohol and contains the precipitin, the smaller remains in the alcoholic filtrate and gives an intensely positive ninhydrin test. The precipitin reaction demonstrates one of the products of proteolysis, the ninhydrin test the other. The fact that animals produce specific precipitins against homologous organ proteins proves the soundness of the Abderhalden principle.

J. D. WILLEMS.

ERRORS AND RISKS IN THE DETERMINATION OF BLOOD TYPES. P. SCHUMACHER and K. ATZERODT, Klin. Wchnschr. **5**:2016, 1926.

Changes did not occur in the blood types of 152 patients subjected to galvanization, diathermy, sacral anesthesia, general anesthesia, foreign protein injections and drug therapy. Frequently a pseudo-agglutination took place which was at once vitiated by the addition of physiologic sodium chloride solution.

J. D. WILLEMS.

THE MILK OF SYPHILITIC LYING-IN WOMEN. HACKEMANN, München. med. Wchnschr. **73**:1743, 1926.

Globulin is present post partum in the milk of syphilitic and nonsyphilitic women in practically equal amounts. From the latter it disappears in six

days, from the former in ten days. The Wassermann reaction of the milk parallels the globulin content, but is independent of the reaction of the blood.

J. D. Willems.

Experimental Infection and Immunization of Young and Old Mice and Guinea-Pigs with Pneumococci and Streptococci Through Feeding and Inhalation. C. Eguchi, Ztschr. f. Hyg. u. Infectionskrankh. **105**:74, 1925.

Eguchi attempted to infect and to immunize young and old mice, also young and old guinea-pigs with pneumococci and streptococci by feeding and inhalation. Young guinea-pigs may sometimes be killed by a single feeding of streptococci or pneumococci. Young mice cannot be infected by mouth, but they may be immunized by feeding them dead pneumococci, type 1. This is not possible in adult animals. Young and old mice may be protected against a 100 times fatal dose by inhalation of sufficient quantities of dead pneumococci, type 1. Young mice could be more readily immunized by feeding dead pneumococci, type 2, than old mice. Similar experiments with pneumococci, type 3, or streptococci (Aronson) were unsuccessful.

W. Ophüls.

Experimental Infection and Immunization by Mouth of Young and Old Mice and Guinea-Pigs with Erysipelas, Mouse Typhus, Typhus and Dysentery. C. Eguchi, Ztschr. f. Hyg. u. Infectionskrankh. **105**:91, 1925.

Eguchi tried to infect and to immunize young and old mice, also young and old guinea-pigs by feeding them the bacilli of swine erysipelas, of typhus murium, of typhoid fever and of dysentery. He found that young guinea-pigs are to some extent susceptible to this mode of infection with the bacillus of swine erysipelas. Young mice were no more susceptible to feeding of these bacilli than old ones. The animals which recovered did not show any considerable immunity. Attempts at immunization of young mice by administration of dead or living cultures of *B. typhosus* were unsuccessful. Similar experiments with Shiga bacilli seemed to produce a slight immunity. No immunity was obtained by feeding mice large doses of bacillus typhi murium and of bacillus typhosus even though the feeding caused death of a large number of experimental animals.

W. Ophüls.

Biologic Differentiation of Rat and Mouse Albumin. R. Otto and E. Cronheim, Ztschr. f. Hyg. u. Infectionskrankh. **105**:181, 1925.

The albumins of the blood of rats and mice may be differentiated to some extent by careful quantitative tests of the active anaphylaxis produced by them.

W. Ophüls.

The Bacteriolysis of Bacillus Tuberculosis. W. Blumenberg and W. Möhrke, Ztschr. f. Hyg. u. Infectionskrankh. **105**:186, 1925.

Different strains of tubercle bacilli show a different solubility. The strain used by the authors could be completely dissolved only in concentrated lactic acid at 37 C. in thirty days, by digestion with pepsin after the bacilli had been treated with benzoylchlorid and by hydrolysis with hydrogen peroxyde in the autoclave at 150 C. in two hours.

W. Ophüls.

CONTRIBUTION TO IMMUNOBIOLOGY OF TRYPANOSOMES. RACIAL AND SPECIES UNITY OF TYPES OF TRYPANOSOMA BRUCEI. H. KROÓ, Ztschr. f. Hyg. u. Infectionskrankh. **105**:247, 1925.

Biologic immune reactions in the case of trypanosomes are specific for the genus only, not for the species. The species can be determined only by testing the pathogenic properties of a given strain on numerous animals.

W. OPHÜLS.

ACTIVE IMMUNIZATION OF UNDERNOURISHED ANIMALS. R. BIELING, Ztschr. f. Hyg. u. Infectionskrankh. **105**:254, 1925.

Undernourished or fasting rats develop a less marked antitoxic immunity than normally nourished animals.

W. OPHÜLS.

CHEMISTRY OF BACTERIAL TOXINS. K. KELLENBERGER, Ztschr. f. Hyg. u. Infektionskrankh. **106**:253, 1926.

When dysentery toxin is mixed with hydrochloric acid under proper conditions, toxicity and antigenic power are reduced in the same degree. When the acid is neutralized the toxin again becomes toxic and antigenic. This parallelism indicates that toxicity and antigenic power reside in the same atomic groups.

THE USE OF THE PRECIPITATION METHOD FOR THE EVALUATION OF SUCH ANTITOXIC DIPHTHERIA SERUMS AS HAVE BEEN SUBJECTED TO THE INFLUENCE OF PHYSICS-CHEMICAL FACTORS. E. HOEN, L. TSCHERTKOW and W. ZIPP, Ztschr. f. Immunitätsforsch. u. exper. Therap. **47**:277, 1926.

A ring precipitation test is described applicable to testing the potency of diphtheria antitoxin. The authors claim that it is a safe and constant demonstration of the antitoxic strength of antidiphtheria serum.

PAUL R. CANNON.

THE DEMONSTRATION OF ANTIGENIC FUNCTIONS OF LIPOIDS IN THE BLOOD SERUM. A. J. WEIL, Ztschr. f. Immunitätsforsch. u. exper. Therap. **47**:316, 1926.

Experiments are described which tend to indicate that there are heterogenetic antigens in horse serum which are demonstrable only by alcohol extraction.

PAUL R. CANNON.

PARA-IMMUNITY. L. SILBER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **47**:347, 1926.

The author describes experiments confirming the observations of previous workers that para-immunity really exists. For instance, rabbits immunized against *Bacillus typhosus*, are also immunized against a paraproteus organism. He suggests that the entrance of a pathogenic organism into the host may exert a special effect on the usual flora, thus complicating the discovery of the etiologic agent.

PAUL R. CANNON.

THE INFLUENCE OF LIGHT ON TUBERCULIN. W. HAUSMANN, W. NEUMANN and K. SCHUBERTH, Ztschr. f. Tuberk. **46**:32, 1926.

Tuberculin in dilutions of 1:100 or more loses much or all of its skin reaction potency after intensive radiation with a mercury vapor quartz light. This action is exerted by rays of 325 microns or less wave length. Concentrated

tuberculin solutions are resistant against light. The destructive action of light on tuberculin dilutions does not have any relation to the curative effect of light on tuberculous lesions.

MAX PINNER.

EXPERIMENTAL STUDIES OF PRECIPITIN AND SPECIFIC CUTI-REACTION: IV. THE RELATION BETWEEN PRECIPITIN AND CUTI-REACTION. GICHU SHOJI, Acta derm. **8**:1, 1926.

Rabbits immunized with egg white or serums (human, horse or sheep) were tested for cutireactions with an injection of 0.1 cc. of antigen in the abdominal region. The reinjection of the same antigen constantly produced a specific dermoreaction which varied directly with the precipitin titer. Exceptions were rare. Individual variations in the intensity of the reaction occurred, and one rabbit tested several times varied in the dermoreaction although the precipitin titer remained unchanged. The intensity of reaction depends directly on the concentration of the injected antigen. The marked irritability of the skin of the immune animal to the specific antigen is shown by reactions to dilutions as high as 1:1,000 or 1:10,000. The reaction is the result of the combination of antigen and precipitin in the cutaneous tissue. The allergic state of the tissue at the same time plays an important rôle, but does not necessarily depend on the existence of precipitin in the blood serum of the animal; the allergic condition may exist for a certain length of time after the elimination of precipitin from the blood stream.

FROM AUTHOR'S ABSTRACT, E. B. PERRY.

RACIAL BIOLOGY IN GREENLAND. E. BAY-SCHMITH, Ugesk. f. Læger **88**:880, 1926.

Of 230 persons 54 per cent belonged to group 1 (Jansky) and 36 per cent to group 2.

Tumors

A CASE OF CARCINOMA OF THE COLON ASSOCIATED WITH SCHISTOSOMIASIS (BILHARZIOSIS) IN A YOUNG WOMAN. BENJAMIN ROMAN and ALICE BURKE, Am. J. Path. **2**:539, 1926.

There is a possibility that the carcinoma developed in consequence of the intestinal schistosomiasis.

A STUDY OF THE TUMOR INCIDENCE IN THE LOWER ANIMALS. W. H. FELDMAN, Am. J. Path. **2**:545, 1926.

The occurrence of tumors in the mule, horse, dog, beef, sheep, swine, mouse, rabbit and chicken is illustrated and discussed.

PRIMARY CARCINOMA OF THE LIVER OF POSSIBLE MULTICENTRIC ORIGIN OCCURRING IN A CASE OF PORTAL CIRRHOSIS. ARCHIBALD H. MCINDOE and VIRGIL S. COUNCELLER, Am. J. Path. **2**:557, 1926.

Two independent carcinoma nodules, one in the right and the other in the left lobe of a liver, the seat of atrophic cirrhosis, are described.

AUTOPSY REPORT OF A CASE OF PRIMARY CARCINOMA IN A DUODENAL DIVERTICULUM. T. H. MORRISON and M. FELDMAN, Ann. Clin. Med. **5**:326, 1926.

The writers consider their case of primary carcinoma—scirrhous—in a duodenal diverticulum to be the only one in the literature. The diverticulum

measured 6 cm. in length and 0.75 cm. in width; at its mouth was an indurated mass the size of a small hen's egg. The growth compressed the hepatic duct. The liver contained numerous metastases.

WALTER M. SIMPSON.

FIBROSARCOMATOUS TUMORS OF THE SKIN OF THE TRUNK CHARACTERIZED BY ATTENUATED DERMAL SURFACES. A. E. HERTZLER, Ann. Surg. **84**:489, 1926.

These tumors grow slowly and remain encapsulated for a long time. The skin over them is reddish or pinkish, attenuated and closely attached to the tumor, which is otherwise encapsulated. The cells are elongated and spindle shaped. At a late stage they invade the skin and then metastasize by the lymphatics. Early excision wide of the capsule is indicated and produces cure.

N. ENZER.

CONCERNING INTRACRANIAL MALIGNANT METASTASES. THEIR FREQUENCY AND THE VALUE OF SURGERY IN THEIR TREATMENT. F. GRANT, Ann. Surg. **84**:635, 1926.

Carcinoma of the lungs and breast metastasize frequently to the brain. In sarcomatous metastases the primary tumor is most frequent in the kidney and the skin. It must be remembered that brain metastases are more common in sarcomas, but that carcinomas are more frequent than sarcomas, hence the greater number of secondary carcinomas of the brain. These metastases are nearly always multiple and involve the brain first, extending later to the meninges. Only one suggestive clinical feature has been observed, and that is a suddenly developing psychosis with a history of a primary malignant focus.

N. ENZER.

MULTIPLE PRIMARY CEREBRAL NEOPLASMS. REPORT OF A CASE. I. J. SANDS, Arch. Neurol. & Psychiat. **16**:447, 1926.

Report of a case of angioma and endothelioma in one frontal lobe. Multiple primary tumors are rare in the brain.

ROY GRINKER.

GIANT CELL TUMOR OF BONE. J. L. GOFORTH, Arch. Surg. **13**:846, 1926.

Four cases of benign giant cell sarcoma are described, emphasis being placed on the stroma. This varied from the mature fibrous tissue matrix to the more cellular fibroblastic and fibrous reticulum. In no instance did these cells show unusual behavior or activity. Another case is reported which recurred after two curettements, and in which the patient finally died with pulmonary metastases. In this case the stroma was cellular with many mitotic figures. The giant cells did not show any change. This case is cited as one of benign giant cell sarcoma undergoing malignant change. A sixth case is described of osteogenic sarcoma, containing giant cells. The author considers that the giant cells are well termed "osteoclasts" and that they function as bone absorbers, and although they possess tumor cell characteristics they are to be regarded as benign. The malignancy of this tumor depends on the character of the stroma, and the presence of the giant cells in metastases probably results from their being carried there by the metastasizing fibroblastic tissue.

N. ENZER.

THE EFFECT OF SODIUM ON THE RATE OF CELL DIVISION. CHARLES PACKARD, J. Cancer Research **10**:1, 1926.

Rats infected with tumor show changes in the amount and proportion in which the cations sodium, calcium and potassium are present. In an actively growing tumor the amount of sodium in the blood is about 25 per cent above the normal; in tumors which regress, the increase in sodium is nearly 60 per cent. The calcium in both instances is constant and the potassium is decreased. Packard is wondering whether these changes in the mineral content of the blood influences the rate of growth of the tumors. For the purpose of investigation of this problem he carried on experiments with *Paramecium caudatum*, in accord with Rohdenburg's statement that the results of tests on a single celled organism should give a clear answer to this question. Packard affirms that it is possible to determine accurately the division rate when these cells are reared in mediums whose chemical composition, in respect to the proportion of sodium, calcium and potassium, is made to resemble as far as possible the two types of abnormal blood.

He arrived at the conclusion that when grown in hay mediums in which the sodium content is above the normal amount, the paramecia show definite changes in division rate. A moderate increase, corresponding to that found in the blood of rats in which a tumor is growing, results in an accelerated division rate. A greater increase, corresponding to the change found in receding tumor blood is followed by a retardation. Packard is of the opinion that the essential difference between the growing and the retarding solutions lies in the change in the ratios between sodium and calcium; variations in the potassium content have little or no effect, the results suggesting that the rate of growth of tumors in rats is associated directly with the ratio between calcium and sodium in the blood.

B. M. FRIED.

THE INHERITANCE BEHAVIOR OF CANCER AS A SIMPLE MENDELIAN RECESSIVE. STUDIES IN THE NATURE AND INHERITABILITY OF SPONTANEOUS CANCER IN MICE. Twenty-first report. MAUD SLYE, J. Cancer Research **10**:15, 1926.

Maud Slye affirms that heredity basically controls every item of the normal and of the pathologic organic response, though the type of inheritance behavior is not alike in all. The present article concerns itself only with the problem of the inheritability of cancer in mice. The conclusions published have been based on over 5,000 primary spontaneous neoplasms, including every type known in human pathology. In every test which the author has conducted on the animals, the cancer resistant and the cancer susceptible tendencies have proved to be inheritable. By the hybridization test the tendency to cancer resistance has proved to be dominant over the tendency to cancer susceptibility, and both these tendencies have proved to be unquestionably inheritable, following with great perfection the mendelian pattern. The types of cancer both primary and secondary, and the locations where they are likely to occur, have also proved to be inheritable, both by the inbreeding and by the hybridization tests, and these characters also have closely followed the mendelian pattern. The author is of the opinion that to all probabilities cancer is similarly inheritable in human beings. There has been, according to the author, in the medical profession a reluctance to accept the fact of the inheritability of cancer, and a preconceived and enduring prejudice against it. "Although," she says, "all workers in the subject have found cancer inheritable, whether they have dealt with spontaneous tumor or with tumors experimentally produced in any one

of many different ways, yet they reject the fact of cancer inheritability for the human species. Such a tenet leads them to the inevitable conclusion that evolution applies up to the human species and breaks there, leaving man unrelated to all other forms of life."

B. M. FRIED.

IODINE IRRITATION DOES NOT PRODUCE CANCER. JULIUS ROSENSTIRN, J. Cancer Research **10**:61, 1926.

Rosenstirn has investigated the effect of aqueous and alcoholic preparations of iodine on the skin of mice known to be susceptible to cancer. Examination eighteen months after the painting showed a local lymphocytic and fibroblastic infiltration. In no instance was even a hyperkeratosis noted.

B. M. FRIED.

CONCERNING GYE'S HYPOTHESIS OF THE ETIOLOGY OF MALIGNANT TUMORS WITH SPECIAL REFERENCE TO THE "SPECIFIC FACTOR." M. J. HARKINS, J. F. SCHAMBERG and J. A. KOLMER, with the assistance of CLARA M. KAST, J. Cancer Research **10**:66, 1926.

Gye stated that all malignant new growths contain an ultramicroscopic organism or virus and an activating substance which he designates the "specific factor." The present investigation concerns itself with an attempt to confirm the cultivation of the virus in vitro and to the demonstration of the "specific factor." The experiments performed throw considerable doubt on the destruction of the infectivity of the "specific factor" prepared according to Gye's technic. The authors could not confirm the evidence of growth of the virus of the Rous chicken sarcoma in subcultures nor could they corroborate the statement that the so-called specific factor acts by reason of the presence of a chemical substance. Their results suggest that the "specific factor" is in reality nothing more than a suspension of attenuated living virus which may or may not produce a tumor, depending on the fowl's susceptibility or resistance.

B. M. FRIED.

THE IMMUNIZATION OF CANCER BEARING MICE. S. ITAMI, J. Cancer Research **10**:115, 1926.

Haaland has failed to immunize mice against their own spontaneous tumor. Itami's experiments were conducted with the carcinoma strain 63. His conclusions are that mice bearing this strain of carcinoma can be immunized as readily as normal animals. Grafts from a tumor growing in an immunized mouse fail in other immunized mice, whether they bear tumors or not. In the mouse itself, however, they are able to grow when inoculated as an intact graft, but not when introduced as a suspension, either into the circulation or into the subcutaneous tissues. The author is of the opinion that a suspension of cancer cells may be a more delicate indicator of resistance, because of the smaller dose administered, than the ordinary block.

B. M. FRIED.

FURTHER INVESTIGATIONS ON THE IMMUNIZING POWER OF NORMAL MOUSE TISSUES AGAINST TRANSPLANTABLE CARCINOMA. S. ITAMI, J. Cancer Research **10**:128, 1926.

Years ago the author tested various tissues in respect to their immunizing power against several transplantable tumors of the mouse and rat. The results obtained at that time were negative with the exception that there seemed to

be some relation between the cellularity of a tissue and its immunizing power, the more cellular tissues appearing to be more active.

The present experiments are a continuation of those previously reported. Itami concludes that resistance to tumor transplantation can be brought about by previous treatment with some, but not all, of the derivatives of all three germ layers. Washed red blood cells are ineffective; leukocytes and lymphocytes do elicit resistance, the latter being somewhat more resistant than the former.

B. M. Fried.

The Lymphocyte in Resistance to Tissue Grafting, Malignant Disease, and Tuberculous Infection. J. B. Murphy, Monographs of the Rockefeller Inst. for Med. Res., no. 21, 1926.

Murphy has gathered together in monograph form the results of fourteen years of experimental studies on the rôle of the lymphocyte in natural and induced resistance to heteroplastic tissue grafts, inoculated tumor, transplanted cancer, spontaneous cancer and experimental tuberculosis. He has brought together in logical fashion the gist of some sixty previously published papers by himself and co-workers.

In heteroplastic tissue grafts, the characteristic round cell infiltration is regarded as a purposeful reaction, and these cells are considered to be the agent through which the mechanism of reaction to foreign tissue grafts exerts itself. The adult organism may be rendered nonresistant to heteroplastic tissue by destruction of the major portion of the lymphoid system and the power to rid itself of the foreign tissue is regained only when the lymphoid tissue has regenerated approximately to the normal amount.

As regards the relationship of the lymphocyte to resistance against transplanted malignant tumor, experimental evidence is presented which indicates that the lymphoid elements play an important part in the process of so-called cancer immunity. When the host is resistant this is evidenced by a local round cell reaction about the graft, a condition entirely absent in the susceptible animal. This local reaction of resistance is accompanied by a great increase in the circulating mononuclears, and back of this, in turn, is an increased proliferation in the lymphogenic centers. On the other hand, the lymphoid tissue of a susceptible animal supporting a growing tumor shows marked degenerative changes which progress with the enlargement of the tumor. Experimentally produced variation in the amount and activity of the lymphoid tissue is accompanied by a variation in the resistance of the animal to cancer; increased activity results in increased resistance.

The mechanism by which the destruction of cancer cells is brought about seems to be the same regardless of whether the tumor is a transplanted one or one which has developed spontaneously.

These studies permitted the author to arrive at certain conclusions regarding the possible effect of roentgen-ray therapy on cancer. Doses of the roentgen ray sufficient to deplete the lymphoid system definitely lower an animal's resistance to implanted tumor. This mechanism may account for those instances in which malignant tumors in man have apparently grown more rapidly and disseminated more freely after intensive roentgen-ray treatment. There is no evidence that cancer cells are more easily destroyed by the roentgen ray than normal cells; the roentgen ray in a mild erythema dose renders the exposed area highly resistant to a subsequent cancer implant; this resistance seems to depend on the amount of cellular reaction induced; the roentgen ray in large generalized doses definitely lowers an animal's resistance to implanted cancer.

The application of similar experimental methods to the study of lymphoid cells in tuberculous infections showed that the degree of resistance has a definite quantitative relationship to the amount and activity of the lymphoid tissue.

WALTER M. SIMPSON.

INSULIN IN NORMAL AND CANCEROUS TISSUES. W. CRAMER, F. DICKENS and E. C. DODDS, Brit. J. Exper. Path. **7**:299, 1926.

Insulin is present in normal tissues in appreciable amounts. It is absent from malignant growths. The cells of normal tissues oxidize dextrose, the cells of malignant growths split dextrose, as Warburg found, with the formation of lactic acid. This parallelism suggests that the oxidation of dextrose by the cells is dependent on the presence of insulin at the site of oxidation.

S. A. LEVINSON.

DIFFUSE ADENO-SARCOMA OF COLON. E. V. PHILLIPS and J. S. MACBETH, Brit. M. J. **2**:524, 1926.

There is described a diffuse carcinomatous infiltration of mucous and submucous coats of colon from cecum to rectum.

TUMORS OF TESTICLE: TERATOID GROUP. F. G. BELL, Brit. J. Surg. **8**:7, 1925.

Bell holds that the majority of testicular tumors belong to the teratoid category. The relative representation of the various blastodermic derivatives varies greatly in different specimens. Overgrowth of one blastodermic element with partial or total (?) suppression of the others occurs frequently. Hypoblastic overgrowth is most common, mesoblastic next in frequency, and epiblastic least common. Such overgrowth may be simple or malignant, and produces many variations from the typical three-layered teratoma. Teratoma testis is potentially malignant to a high degree.

"SARCOMA OF THE PROSTATE IN AN INFANT OF NINE MONTHS." M. LAQUIÈRE and R. BOUCHARD, J. d'urol. **22**:244, 1926.

An infant of 9 months presented the clinical signs of prostatic enlargement. At operation for the drainage of a supposed abscess, the prostate was found to be enlarged, hard and white. Biopsy confirmed the operative diagnosis of sarcoma. The infant died ten days after the operation. Autopsy showed the prostate to be completely invaded by sarcoma of the spindle cell type.

WALTER M. SIMPSON.

ACUSTICUS NEURINOMA. G. L. DERMAN, Virchows Arch. f. path. Anat. **261**: 39, 1926.

Derman describes four examples of tumor of the cerebellopontile angle, none of which was associated with generalized neurofibromatosis. The characteristic palisade arrangement of the nuclei led the author to conclude that the tumors were neurinomas.

O. T. SCHULTZ.

GASTRO-INTESTINAL NEUROFIBROMATOSIS. D. BANERJEE and E. CHRISTELLER, Virchows Arch. f. path. Anat. **261**:50, 1926.

Intestinal neurofibromatosis is subdivided into (1) that which is part of generalized neurofibromatosis; (2) that limited to the intestine alone; (3) that

which is associated with sarcomatous change; (4) localized intestinal neurofibromatosis associated with localized overgrowth of the intestinal wall. The authors report two adults with generalized neurofibromatosis and intestinal involvement. The first patient, a man, aged 44, died following an operation for tumor of the brain. In addition to nodules of the skin, peritoneum, small intestine and stomach there was a firm tumor mass, 5.5 cm. in diameter, in the right cerebral hemisphere. On microscopic examination the tumor was found to have the same structure as the other neurofibromatous nodules and was considered to be an intracerebral neurofibroma. This unusual situation of the tumor is explained on the basis that neurofibromatosis is a blastomatous maldevelopment of the nervous system and may give rise in the central as well as in the peripheral nervous system to overgrowths which may vary in their tissue composition. In the second patient, a woman, aged 54, a neurofibromatous nodule of the jejunum has led to intussusception and intestinal obstruction.

O. T. SCHULTZ.

MUCOUS CELL CARCINOMA OF THE PANCREAS. K. HELLY, Virchows Arch. f. path. Anat. **261**:68, 1926.

A cylindric cell carcinoma of the pancreas, reported by Helly, was believed to have arisen from mucous secreting cells which occur normally in the lining epithelium of the ducts.

O. T. SCHULTZ.

VARIATIONS IN RESISTANCE TO EXPERIMENTAL TAR CANCER. K. YAMIGIWA, T. FUKUDA, Y. KANEKO and T. AZUMA, Virchows Arch. f. path. Anat. **261**:75, 1926.

The production of epithelioma of one ear of the rabbit following repeated application of tar did not have any effect on the later development of a similar tumor of the other ear as the result of the same procedure. In mice with tar cancer it was possible to inoculate successfully a heterologous tumor (carcinoma of the mammary gland), but the growth of the latter was indirectly proportional to the rapidity of growth of the tar cancer. The application of tar at varying intervals after extirpation of an inoculated mammary carcinoma was followed by the formation of epithelioma. In mice which gave negative results after repeated inoculations of mammary carcinoma, tar cancer could be successfully produced. All of the results indicate that epithelioma caused by tar does not bring about a refractory state against either homologous or heterologous tumors and that a heterologous type of tumor does not bring about any resistance to the tar cancer.

O. T. SCHULTZ.

HEMANGIO-ENDOTHELIOMA OF THE LIVER. A. BLUMBERG, Virchows Arch. f. path. Anat. **261**:82, 1926.

Blumberg reports a tumor of the liver, in a man, aged 51, which he terms a hemangio-endothelioma. The neoplasm formed wide blood filled spaces, lined by proliferating endothelium, and narrow, solid cords of cells which grew along the liver sinusoids. The cells of the solid cords were like the Kupffer cells, from which the author conceives the tumor to have come, the angiomatous portion arising by differentiation from the solid portions.

O. T. SCHULTZ.

PRIMARY ENDOTHELIOMA OF THE LUNG. F. BATTAGLIA, Virchows Arch. f. path. Anat. **261**:87, 1926.

Battaglia describes a localized solid tumor of the lower lobe of the left lung of a man, aged 67. Microscopically the tumor was cellular and alveolar in character, and had the appearance of a carcinoma. The lymph node metastases, however, were composed of elongated spindle cells, which did not have an alveolar arrangement. The metastases had the appearance of sarcoma. The author excludes the possibility of the existence of two primary tumors and believes that the formation of both sarcomatous and carcinomatous tissue is evidence in favor of the lymphendotheliomatous origin of the tumor, supporting his argument by the belief that endothelium has epithelial characteristics, in that it covers surfaces, and mesoblastic characteristics, in that it can form connective tissue.

O. T. SCHULTZ.

LATE RECURRENCE IN CANCER OF BREAST. ULRIK QUENSEL, UPSALA LÄKAREF, Füh. **31**:553, 1926.

In a woman, aged 64, local recurrence developed fifteen years after removal of the breast for cancer. The recurrent growth, the size of a hazelnut, was a simple carcinoma with mammary tissue at the periphery. It is conceded that the second cancer arose in mammary tissue not removed at the original operation.

Medicolegal Pathology

THE QUANTITATIVE DISTRIBUTION OF VERONAL IN THE ORGANS IN A CASE OF VERONAL POISONING. W. G. PUCHER, Bull. Buffalo Gen. Hosp. **3**:70, 1925.

The following amounts of barbital (veronal) were recovered from the organs and urine of the patient whose case is reported. [The fatal dose consisted of about twenty 5 grain (0.3 Gm.) tablets.]

Substance Analyzed	Total Weight	Barbital per 100 Gm.	Barbital in Total Weight
Urine (obtained from bladder p. m.)	328 gm. (320 cc.)	84 mg.	276 mg.
Liver	1,200 gm. (estimated)	12.8 mg.	154 mg.
Brain	1,400 gm. (estimated)	14.0 mg.	196 mg.
Kidneys	242 gm.	19.4 mg.	47 mg.
Spleen	140.5 gm.	12.1 mg.	17 mg.
Gallbladder	17.0 gm.	.....	5 mg.

Total barbital recovered, 695 mg.

The results confirm the observation of other investigators that most of the barbital is to be found in the urine. The other organs, however, contain appreciable quantities particularly the liver, kidney, brain and spleen. Calculated on the basis of barbital per hundred grams of tissue, it is found that the kidney is the highest and the brain next in barbital content. AUTHOR'S SUMMARY.

A DISTINCT PATHOLOGICAL LESION IN DEATHS FROM HIGH VOLTAGE ELECTRIC CURRENT. K. SELLERS KENNARD, Med.-Leg. J. **43**:14, 1926.

In four persons who died from electric currents of high voltage, and in three dogs killed by such current experimentally, marked fragmentation of the myocardium was observed.

THE LEGAL RELATION OF THE AUTOPSY. K. SELLERS KENNARD, New York State J. Med. **26**:390, 1926.

This article gives a general summary of the laws and decisions in the state of New York concerning the right of physicians to make postmortem examinations.

ELIMINATION OF ERRORS IN DETERMINATION OF BLOOD GROUPS. M. KERNBACH, Ann. de méd. lég. **7**:1, 1927.

It is recommended that in testing for blood groups, the red corpuscles used should be washed first in physiologic salt solution. By so doing pseudo-agglutination, auto-agglutination and panagglutination will be eliminated.

CYSTODIAGNOSIS OF BLOOD SPOTS IN SITU. NERIO ROJAS and CARLOS DANIEL, Ann. de méd. lég. **7**:84, 1927.

Good results are reported from the microscopic examination of blood stains in situ. The area containing the spot is fixed in alcohol and ether, equal parts, and then stained in hematoxylin and eosin. A piece of paper with a blood spot on it may be treated as if it were a celloidin section. When it concerns opaque material, lateral illumination is used (epimicroscope) for the microscopic examination.

A CASE OF DIAGNOSIS OF THE INDIVIDUAL FROM BLOOD SPOTS. LEONE LATTES and GIORGIO CANUTS, Rass. internaz. di clin. e terapia **7**:248, 1926.

The question arose whether blood on the clothes of a person suspected of murder corresponded to his blood group or not. It was claimed that the blood was due to nose bleed in the suspect. The blood of the suspect belonged to group *O* and the extracts of the blood on the clothes did not agglutinate his corpuscles but did agglutinate the corpuscles of groups *A* and *B*; furthermore, absorption experiments with serum of group *O* and the blood spots gave negative results. As the blood on the clothes and the blood of the suspect were found to belong to the same group, the conclusion was drawn that the spots in question might have been made by the blood of the suspect. The spots in this case were at least two months old.

DETERMINATION OF SEX BY MONOILOFF'S REACTION. G. ALTERBERG and A. HAKANSSON, Biochem. Ztschr. **176**:251, 1926.

In 1924 Monoiloff described a complicated chemical color reaction, making use of five different reagents, the outcome of which was believed to make it possible to detect the male or female origin of blood or any other material. This reaction was held to be of universal biologic application and to be capable of differentiating the origin of substances of plant as well as animal origin. This contention, if established, would make the reaction of the utmost forensic importance. The authors working at the University of Lund, investigated the various factors which enter into the reaction and the outcome of the reaction itself. They found that the relative proportion of the extracted material to be tested was an important factor in the reaction, that specific enzyme activity did not play any part, and that the result obtained was due in part at least to reduction and oxidation reactions brought about by the materials used. They conclude that the reaction has only a quantitative and not a qualitative application, and that it has no forensic value in helping to determine the male or female origin of any suspect material.

O. T. SCHULTZ.

THE ENTRANCE OF THE CURRENT IN ELECTRIC DEATH. H. SCHRIDDE, Deutsche med. Wchnschr. **52**:1607, 1926.

In 102 cases the current entered the head fourteen times and the hands eighty-eight times. In the series of cases in which the current entered the hands, it appeared that the point of entrance was in the left hand in 87.53 per cent and in the right hand in 12.47 per cent. Schridde regards electric death as essentially a cardiac death; when the current enters the head, it makes its way to the feet through the heart.

THE DETERMINATION OF ALCOHOL IN FORENSIC MEDICINE. M. H. REMUND, Schweiz. med. Wchnschr. **56**:909, 1926.

Remund discusses the medicolegal significance of the quantitative determination of poisons, especially of alcohol, in the blood, brain and other organs. The alcohol concentration in the body rapidly changes, in life by oxidation and elimination through the lungs and skin, in death by autolysis, putrefaction and evaporation. The lay diagnosis of drunkenness is frequently wrong, as nervous excitement and loss of muscular control are symptoms shown by other poisons. The alcoholic odor is a better aid in arriving at a diagnosis than the other symptoms. However, the finding of alcohol does not necessarily imply drunkenness, as the alcohol may have been administered therapeutically. The detection of alcohol in cadavers is frequently of great importance, as it may concern cases involving large amounts of insurance. The alcohol content of the organs and of the blood cannot be detected by the odor, even when death follows the taking of large quantities of alcohol. Remund reports a series of cases from the Zurich Institute of Legal Medicine in some of which the diagnosis was impossible, since the alcohol concentration could not be determined, autopsy having been made eight days after the alleged intoxication. He believes that there are many errors committed in diagnosing alcoholism by the present methods and that there is a need of more accurate procedures. [In New York, Chicago, Boston, etc., laboratories are available for the medical examiner or coroner's physician for chemical examinations for alcohol, so the presence or absence of alcohol can be determined by chemical means.]

W. D. MCNALLY.

DETECTION OF ETHYL ALCOHOL. FRITZ SCHWARZ, Schweiz. med. Wchnschr. **56**:923, 1926.

Schwarz gives a detailed description and criticism of the various methods of determining alcohol in biologic material and organs. The alcohol is recovered by steam distillation and then redistilled one or more times to free it from volatile acids and decomposition products. Following this the alcohol is determined by the oxidation method of Nicloux or one of the modifications of this method. The process of oxidation introduces errors as a result of the formation of aldehydes, acid and carbon dioxide, depending on the conditions of the reaction. If the reaction mixture is heated for a definite length of time the errors are largely overcome. As a check on the amount of alcohol found, the interferometer method may be used. This method has a sensitivity of 0.0003 per cent alcohol. The odor of the breath should not be taken as evidence of drunkenness, but some chemical method should be used for the detection of alcohol. If the breath is allowed to bubble through an alkaline solution of iodine in potassium iodide the formation of iodoform indicates alcohol in the breath. It is important to take the material for analysis as soon as possible, since the alcohol is burned in the organs as well as given off in the breath. According to Nicloux, the alcohol concentration in the blood begins to fall

after two hours and is half gone after from five to eight hours, and only traces are left after fifteen hours. Methyl alcohol remains longer. A post-mortem examination should be made as soon as possible and samples should be placed in clean vessels to avoid contamination with reducing substances or bacteria. Caution must be exercised in taking case histories. Alcohol might be a factor in causing death, even though other poisons are present. Fifty-eight references are included in the bibliography. W. D. McNally.

Bromine Distribution in Bromide Poisoning. E Vilén, Upsala Läkaref. **31**: 373, 1926.

Vilén presents the case of a man who had taken 100 Gm. of sodium bromide in less than two days. Qualitative determinations of bromine in the urine, blood, spinal fluid, stomach contents and serum of cutaneous blisters, made while the patient was alive, were all positive. After the necropsy, the bromine content of all the organs was determined quantitatively by means of Volhard's titration method, after destruction of organic substances with sodium hydroxide and sodium nitrate. The greatest amounts of bromide were found in the cerebral cortex, lungs and kidneys, in which organs it varied between 0.3 and 0.5 per cent. The gray matter of the cerebrum contained twice as much bromine as the white matter, the basal ganglions or the cerebellum.

Technical

A Dye-Method for Determining the Blood Volume in Man. J. Lindhard, Am. J. Physiol. **77**:669, 1926.

Using intravenous injections of vital red, with certain definite precautions, the writer was able to obtain blood volumes in the human being agreeing, in double determinations in the same person, within 0.2 liter. The precautions were:

Use of a minimum amount of recently prepared dye.

Avoidance of dilution of the blood samples.

Preliminary spectroscopic examination of blood samples to rule out possible hemolysis.

Determination of blood volume in the postabsorptive stage, to eliminate the turbidity caused by lipemia.

Active exercise for about five minutes before the withdrawing of both samples.

It is the last precaution that the writer particularly emphasizes, as a necessity in securing uniform mixing of the injected dye with the blood, particularly as concerns that in the cutaneous veins.

Repeated injections of the dye sooner or later result in its elimination from the circulation so that then the method becomes fallacious. At most from five to six determinations may be made in the course of a year.

H. E. Eggers.

Results of 2800 Microscopic Slide Precipitation Tests for Syphilis with Clinical and Serologic Comparison. B. S. Kline, L. Littman and A. B. Mill, Am. J. Syph. **10**:636, 1926.

More than 2,500 slide tests for syphilis show that this test agrees well with the patient's condition and with the Wassermann and Kahn tests. It is more

sensitive than the Wassermann test in early syphilis and treated syphilis. It is simple, it requires little apparatus and serum, and the result is easier to read than in the regular Kahn test.

A Satisfactory Method for Staining the Nerve Fibers of the Iris. M. Balado, Arch. Neurol. & Psychiat. **16**:442, 1926.

The eyeball is fixed in a 10 per cent solution of liquor formaldehydi for twenty-four hours. It is then cut transversely and the choroid and iris carefully detached from the sclera. The iris is washed in water for twenty-four hours, placed in 10 per cent gelatin for twenty-four hours and then placed in 30 per cent gelatin for twenty-four hours. In a pasteboard box the iris is allowed to harden in 30 per cent gelatin in the icebox. The box is detached and the embedded iris is placed in 10 per cent formalin for twenty-four hours. Frozen sections are made and fastened to slides. The sections are then covered with celloidin and placed in 70 per cent alcohol for fifteen minutes. The sections are placed for twenty-four hours in a 1:50 potassium permanganate solution, rapidly washed in water and decolored in 1 per cent oxalic acid for twenty minutes or until white. For two hours the sections are placed in 2.5 per cent pure ferric ammonium sulphate, rapidly washed and stained in Heidenhain's hematoxylin for twenty-four hours. They are then differentiated in the ferric ammonium sulphate, dehydrated and mounted.

Roy Grinker.

Quantitative Estimation of Albumin in Urine. A. M. Moody and S. Stocking, California & West. Med. **25**:359, 1926.

Moody and Stocking detail method for the quantitative estimation of albumin in the urine: In a graduated centrifuge tube of 15 cc. capacity is placed 10 cc. of urine to be tested, and in another similar tube 10 cc. of standard serum solution; then to each tube is added 5 cc. of Tsuchya's reagent (phosphotungstic acid, 15 Gm.; hydrochloric acid, 50 cc., made up to 1,000 cc. with 95 per cent alcohol). This is mixed thoroughly by inverting back and forth and let stand for ten minutes, and then the tubes are placed in the centrifuge and centrifugalized for from three to five minutes. The amount of precipitate in each tube is recorded and the result calculated. The standard tube reading equals 6 Gm. of albumin per liter.

The Excretion of Lead by Normal Persons. Robert A. Kehoe, Graham Edgar, Fred Thamann and Lester Sanders, J. A. M. A. **87**:2081, 1926.

In a series of sixty-five apparently normal, healthy workmen, chosen at random and found to be secreting lead in the feces or urine or in both, not one was suffering from lead poisoning.

There are certain unknown means of exposure to lead so widespread that most persons have absorbed appreciable quantities, as evidenced by their secretion of lead.

There is no diagnostic value in qualitative lead determinations in the excreta of persons suspected of having lead poisoning.

There is at present no quantitative expression of lead secretion in man which may be said to be significant of impending or present lead poisoning.

Authors' Summary.

MICRO-KAHN REACTIONS. R. L. KAHN, J. A. M. A. **87**:2092, 1926.

Micro-Kahn reactions with minute amounts of serum, such as a drop or less, can be carried out with a high degree of accuracy. Both qualitative and quantitative microprocedures can be employed. Such procedures should prove of help to physicians in cases in which it is difficult to obtain sufficient blood for regular Kahn tests.

AUTHOR'S SUMMARY.

A NEW METHOD FOR STAINING ELASTIC FIBERS. JOSEPH M. THURINGER, J. Lab. & Clin. Med. **11**:89, 1925.

To obviate certain objections to the usual methods for staining elastic fibers, Thuringer has devised the following stain: (*a*) Place sections in 0.5 per cent. phosphotungstic acid for five minutes. (*b*) Rinse well in distilled water. (*c*) Stain deeply in Mann's hematin from three to five minutes. (*d*) Differentiate in 2.5 per cent. acetic acid in water. (*e*) Rinse in distilled water. (*f*) Stain with eosin. (*g*) Dehydrate and clear. The procedure varies from a routine hematoxylin-eosin stain only in the preliminary treatment of the sections in 0.5 per cent. phosphotungstic acid solution in water.

The elastic fibers are stained deep blue and appear in great contrast to the general pink of the remainder of the section. The nuclei stain red but are unobstructive. The chromatin granules vary from light brown to blue. The elastic lamina of arteries show beautifully, as well as the most delicate elastic fibers scattered throughout the tissue.

Delafield's hematoxylin may be used if it is desired to show nuclei with greater contrast. Hansen's hematoxylin is especially recommended if a brilliant nuclear stain is desired at the same time. The contrast between the elastic fibers and other tissue elements, however, is greatly diminished.

Phosphomolybdic acid must not be used in place of phosphotungstic acid, since its "affinities" lie more in the direction of the collagen fibers which stain very deeply with the hematoxylin after preliminary treatment with dilute solutions.

The formula for Mann's acid hematin is as follows: hematin, 1.25 gm.; glacial acetic acid, 10.00 c.c.; glycerol, 100.00 c.c.; absolute alcohol, 100.00 c.c.; potassium-alum sulphate, 10.00 gm.; water, 100.00 c.c.

STUDIES IN TOXICOLOGIC CHEMISTRY. V. E. LEVINE, J. Lab. & Clin. Med. **11**:815, 1926.

Selenious acid (or its alkali salts) dissolved in pure concentrated sulphuric acid forms a colorless reagent yielding a characteristic color reaction specific for the phenol group. The color test is extremely sensitive and possesses wide applicability. It is given by monophenols, monophenolic ethers, monophenols with halogen, amino, alcohol, aldehyde or carboxyl group, diphenols and their derivatives like ethers, etc., triphenols, phenolic glucosides and phenolic alkaloids. The intensity of the reaction is modified by the presence of various substituents besides the phenolic hydroxyl in the benzene nucleus. The presence of one or more nitro groups interferes with the reaction completely. The selenious sulphuric acid reagent of Mecke, Lafon and others gives the reaction characteristic of the morphine alkaloids because of the presence of the free phenolic hydroxyl or of one liberated by the interaction of sulphuric acid with one or more methoxyl groups present. Mecke or Lafon's test is not distinctive of the morphine alkaloids. In toxicologic examination of

tissue the author calls attention that phenol, p-cresol, tyrosine, pyrocatechin, hydroquinone and epinephrine are phenolic compounds of biologic occurrence. A positive test is of no absolute significance, but a negative test is important as a conclusive indication of the absence of the morphine alkaloids. The selenious sulphuric acid reagent also serves to differentiate alpha-naphthol from beta-naphthol, and glacial acetic acid from acetic anhydride.

S. A. Levinson.

The Rapid Determination of Albumin in Urine. F. B. Kingsbury, C. P. Clark, G. Williams and A. L. Post, J. Lab. & Clin. Med. **11**:981, 1926.

An improved sulphosalicylic acid nephelometric or turbidimetric method with permanent standards is described. This method is of sufficient accuracy for use in the collection of data in the routine examination of urines for the smaller amounts of albumin.

S. A. Levinson.

Uric Acid Studies: I. Comparison of Direct and Isolation Methods of Determination in Blood Filtrates: Modification of Folin's Method. R. v. E. Wiener and H. J. Wiener, J. Lab. & Clin. Med. **11**:1035, 1926.

A modification of the Folin method for determination of uric acid, which eliminates the danger of precipitation in the reaction mixture and produces a color which is stable for twenty-four hours, is described. It is adapted to determination of uric acid in the urine. The blue, which is produced by resorcinol and phenol when Benedict's or Folin's reagent is used and with tyrosine also when Benedict's reagent is used, is not given by the silver lactate which is used for preliminary isolation of uric acid in this method. Recovery of uric acid from known solutions varied between 95 and 100 per cent.

Ruth Taylor.

Simplified Method for Blood Sugar Estimation. Taken from a Review of Recent Advances in the Study of Blood Sugar and Diabetes. Arthur Dighton Stammers, Physiol. Rev. **6**:672, 1926.

The proteins of the blood (0.2 cc.) are precipitated by heating in the presence of acid sodium sulphate and treatment with dialyzed iron (Maclean's method). Twenty cubic centimeters of the protein-free filtrate are transferred to a boiling tube, two drops of 20 per cent sodium hydroxide and 1 cc. of 0.0075 per cent methylene blue are added and the mixture is boiled. Immediately when vigorous boiling commences, the time is noted and the boiling allowed to proceed as briskly as possible until the blue disappears from the solution, when the time is again noted. Disappearance in 37 seconds indicates 0.3 per cent sugar; 60 seconds, 0.225 per cent; 1 minute, 25 seconds, 0.175 per cent; 1 minute, 55 seconds, 0.125 per cent; 2 minutes, 45 seconds, 0.075 per cent, etc., a graph being used to calculate the result.

If it is merely desired to know whether the blood has a normal concentration of sugar or not, the boiling should be allowed to continue for 2½ minutes; if at the end of this time the blue has not disappeared, the sugar percentage is below 0.1.

Particular attention must be paid to accurate weighing and measurement of the methylene blue, and the boiling must be as vigorous as possible.

Society Transactions

CHICAGO PATHOLOGICAL SOCIETY

Regular Monthly Meeting, Jan. 10, 1927

LLOYD ARNOLD, *President, in the Chair*

ANEURYSM OF THE RENAL ARTERY. HARRY A. SINGER.

Although an aneurysm of a renal artery is manifestly uncommon, it occurs far more frequently than the collected statistics dealing with the subject suggest. The discrepancy between the actual number reported and the number so listed is due mainly to the lack of uniformity in titles, for not an inconsiderable number of reports are made under headings which express the cause, such as periarteritis nodosa, or the effect, as perirenal hematoma, of a renal aneurysm. On this account many reports which rightfully should be included are inadvertently omitted in summaries designated as "aneurysm of the renal artery."

The following two reports are of particular interest in that they illustrate the value of microscopic examination in determining the presence of a renal aneurysm when the etiology is obscure.

CASE 1.—A woman, in the late fifties, without apparent cause had a sudden pain in the right loin followed by hematuria. By cystoscopic examination it was determined that the blood came only from the right kidney. After repeated attacks of pain and hematuria had markedly impaired the health of the patient, surgical intervention seemed advisable. A perirenal hematoma was found, and because the source of hemorrhage was not demonstrable, a nephrectomy was performed. The kidney was sent to Dr. R. H. Jaffé, who found by careful dissection a periarterial hematoma which had its origin in a perforation of one of the interlobar branches of the renal artery. The opening in the vessel communicated with a major calyx on one side and the perirenal tissues on the other. Grossly, the main renal vessel showed the usual changes of atherosclerosis, while the kidney itself had the characteristic changes of arteriosclerotic atrophy. In microscopic preparations of cross-sections of the artery opposite the rupture, the intima was practically normal, but the media was greatly altered. The latter had twice the normal thickness and was irregular in structure, the smooth muscle fibers being distributed in various planes and separated by considerable fibrillar connective tissue. Elsewhere there were no noteworthy changes. It was clear from the microscopic examination that the important factor in the perforation was an alteration of the media. Because of the meager history, it was not possible to account for the vascular changes, but they were presumably due to a previous infectious disease, probably nonsyphilitic.

CASE 2.—A white woman, aged 46, complained of recurrent attacks of severe abdominal pain and persistent vomiting. She had an abdominal mass on the right side, extending posteriorly to the loin. A rapid and continued increase in size suggested that active hemorrhage was occurring. The flow of urine from the right kidney was diminished, as was determined by cystoscopic examination. In the absence of trauma a preoperative diagnosis of perirenal

hematoma of undetermined etiology was made. By a surgical operation an extensive perirenal hematoma was demonstrated. It was caused by a perforation of the right renal artery at a place just distal to its origin from the aorta. To control the hemorrhage while removing the kidney, it was necessary to clamp the artery where it was ruptured and to divide the vessel distal to the defect. Grossly, the extirpated kidney was not changed except for recently clotted blood about its convexity and the presence of a rather firm, grayish-red material which was thought, at the time, to be organizing blood. The larger renal vessels had a patchy intimal sclerosis, although the smaller radicals were unchanged. The portion of the vessel containing the perforation was not removed during the operation. Microscopically, the changes in the sections of the firm tissue found at the root of the kidney were remarkable. The alterations consisted of cellular infiltrations and granulation tissue involving the fat of the hilum together with numerous peculiar vascular structures. These vessels had walls of various thicknesses, some a single layer of endothelium, others moderately thick concentric layers af healthy tissue, while still others were exceedingly thick, and many were slightly or markedly altered by fibrinoid necrosis. The changes here were interpreted as being due to a subacute or chronic inflammation, the source of which is uncertain.

Of particular interest in connection with the reports presented is the etiology. For purposes of classification the causes of an aneurysm of a renal artery may be traumatic and nontraumatic. The latter group can be further subdivided into primary disease of the arterial wall, either degenerative (arteriosclerosis) or inflammatory (syphilis, periarteritis nodosa), and secondary, due to the extravascular disease. Trauma is the cause of an aneurysm of the renal artery in approximately 50 per cent of the reports on record. With many of these the accompanying arteriosclerosis is an important factor, and the trauma, which often is insignificant, is only the exciting cause.

Skin Reactions with Coccidioidal Granuloma. Edwin F. Hirsch. (From the Henry Baird Favill Laboratory of St. Luke's Hospital, Chicago, Ill.)

Broth culture and synthetic medium filtrates of *Coccidioides immitis* injected in animals infected with *Coccidioides immitis* and in a patient with coccidioidal granuloma, cause reactions in the skin resembling those occurring with tuberculin in tuberculous animals. The immediate reaction of the skin is like an urticarial wheal; the delayed reaction is a red swelling of the skin, at its maximum usually within from twenty-four to forty-eight hours after the injection. Heating at 80 C. for thirty minutes does not destroy the activity of these filtrates. Two volumes of 95 per cent alcohol added to one of the filtrate flocculates a substance with active properties that can be dried and powdered. It contains from 3 to 4 per cent nitrogen and, on hydrolysis, from 20 to 40 per cent reducing sugar measured as dextrose.

A complete report will be published with Harriet Benson and Dorothy D'Andrea in the *Journal of Infectious Diseases.*

Acute Intestinal Obstruction in a New-Born Infant From Hernia of the Lower Ileum Through a Congenital Mesenteric Opening. Esmond R. Long, University of Chicago.

Intestinal obstruction from herniation of part of the bowel through a congenital mesenteric opening has been described as "unusual but not rare." Anatomists refer to the condition without mentioning specific instances. Both

Treves and Davis in their textbooks on anatomy state that occasionally congenital defects are found in the mesentery, through which part of the bowel may slip with subsequent strangulation. The most recent report on the anomaly is that of G. D. Cutler (*Boston M. & S. J.* **192**:305, 1925), who reviewed twenty-seven reports of this disorder and added one of his own.

All of these came to the attention of surgeons as typical intestinal obstruction, with a history of three or four days, as a rule, of pain, vomiting and obstipation. The exact nature of the obstruction was not correctly diagnosed in any patient before operation. The age incidence of the patients varied from 1 to 70, the condition occurring more often during youth and a few times in infancy. Operation disclosed herniation of from a few inches to several feet of bowel through slitlike openings, usually close to the ileocecal junction, varying from 5/8 of an inch to 3 inches (1.5 to 7.6 cm.) in length, with strangulation or volvulus. Bloody fluid was found in the peritoneal cavity in all patients, and frequently the strangulated bowel was gangrenous. The operative aim was either reduction or resection. In spite of operation in the cases reviewed, the mortality was over 50 per cent. In general, the mesenteric defects were believed to be of congenital origin, although there was a history of trauma in a fourth of the cases.

The subject of this report was a boy, aged 4 days, a patient of Dr. J. P. Graf at St. Bernard's Hospital. The infant was born of a normal mother, in an easy, normal delivery. It was noted at the time of birth that the infant had a peculiar "froglike" shape. The abdomen was abnormally large, and the thorax was abnormally wide at its junction with the abdomen. The baby took the mother's breast readily, receiving a little water in addition to colostrum from the breast. No bowel movements occurred. The night nurse thought she recollected one passage of meconium, but was uncertain; in view of the condition of the colon found at necropsy, it was almost certain that no meconium ever passed. The abdominal swelling increased, and on the third day castor oil and an enema were given, but had no effect. Following every attempt to nurse after this, the child vomited. A diagnosis of intestinal obstruction, possibly intussusception, was made, and an operation was performed on the fourth day. The peritoneal cavity was found to be full of bloody fluid, and a large loop of bowel without mesentery was seen. The prognosis seemed hopeless, and as the infant was almost moribund, the wound was closed without further manipulation. The child died two hours later.

Necropsy was performed the same day. The abdomen was greatly distended, and the thorax was short, with a broad base, having the configuration of a short cone. There was a slight icterus. Except for these abnormalities and the laparotomy incision, there were no important external changes. Internal abnormalities were found only in connection with the alimentary tract. The peritoneal cavity contained bloody fluid. The stomach and duodenum were normal. The upper jejunum was normal, except for hemorrhage between the leaves of the mesentery. The lower jejunum and upper ileum were enormously dilated and filled with salvelike, green meconium. For a length of 30 cm. the average circumference of the bowel in this location was 15 cm. The ileum tapered gradually to normal size at the lower end of the dilated part. Beginning 15 cm. below the most dilated portion there were numerous fenestrations of the mesentery along a bowel length of 15 cm., extending to within 4 cm. of the ileocecal junction. The last 35 cm. of ileum had passed through one of these openings and was twisted. The coils of this part were drawn tightly together and were almost empty. The entire colon was collapsed and

was free from meconium. Smears of the meconium from the distended part disclosed the typical gram-negative flora of the new-born infant before establishment of the mother's milk supply.

The cause of the fenestration which permitted the hernia with volvulus and intestinal obstruction could not be determined with certainty. In view of the peculiar configuration of the infant's abdomen with pressure deformity of the thorax, noted at birth, it may be assumed that the obstruction took place during intra-uterine life. Whether the fenestration resulted from an embryonic defect or intra-uterine tearing it was not possible to determine. Certainly trauma had added to the extent of fenestration during or after birth, because normal development of the intestinal wall could not have occurred with such extensive loss of mesentery and blood supply as was found at the necropsy. Probably the extreme distention and stretching of the bowel as a result of the obstruction had added to the tearing of the delicate mesentery, with hemorrhage, leading to the hemoperitoneum noted.

It is interesting to speculate on the effect of intestinal obstruction before and after the advent of bacteria in the bowel. Possibly the bacterial flora, which developed after food and water were taken by mouth, played a part in the symptoms attending the intestinal obstruction.

HEMOCHROMATOSIS AND PRIMARY CARCINOMA OF THE LIVER. D. K. HIBBS. (From the Henry Baird Favill Laboratory of St. Luke's Hospital, Chicago.)

Primary carcinoma of the liver associated with cirrhosis is relatively common and seems to occur with the pigment type of cirrhosis more often than is recognized generally. Karsner's review (*Arch. Int. Med.* **8**:238 [Aug.] 1911) mentions cirrhosis in all livers with a primary carcinoma, and of the 107 reports of primary carcinoma of the liver reviewed by Winternitz (*Johns Hopkins Hosp. Rep.* **17**:143, 1916), cirrhosis was present in 87 per cent. Rowen and Mallory (*Am. J. Path.* **1**:677, 1925) reported nine primary carcinomas of the liver in 6,506 postmortem examinations. Seven of the nine carcinomas were of the liver cell type, and six of these occurred in livers with marked cirrhosis. The cirrhosis in three cases was of the pigment type, in three others the alcoholic type. Rowen and Mallory believe that a progressive necrosis of liver cells is accompanied by regeneration, which finally results in cells proliferating indefinitely, as in a malignant tumor.

The cases of three of the sixteen patients with hemochromatosis examined postmortem at the Boston City Hospital during the last twenty-six years are reported by Mills (*Arch. Int. Med.* **34**:292 [Sept.] 1924). These patients are said to have died because of a coincident primary carcinoma of the liver, a sequence which he considers to be relatively frequent. These lesions arise, according to Mills, because of the continual necrosis and regeneration of liver cells, which finally exceed their normal growth limits and proliferate as a carcinoma. Blanton and Healy (*Arch. Int. Med.* **27**:406 [April] 1921) report hemochromatosis in four patients, one of whom had a primary carcinoma of the liver.

M. H., a white man, aged 64, was brought to St. Luke's Hospital, Chicago, in an ambulance. He seemed well until the afternoon of admission, when he suddenly collapsed while at work and became unconscious. At the time of admission he had symptoms of a cerebral hemorrhage or thrombosis, and he died on the following day. The postmortem examination (by Dr. Edwin F. Hirsch) showed that death was due to a huge spontaneous intrapontile hemorrhage. A pigment cirrhosis and a primary carcinoma of the liver, with tumor

tissue thrombosis of branches of the portal vein near the carcinoma were also found. The liver with the empty gallbladder weighed 2,900 Gm. It was dark red-brown, with a capsule finely nodular and roughened by depressed regions of fibrous tissue. The substance of the liver was leathery. On surfaces made by cutting, the lobular markings generally were obscured, and the tissue contained yellow-gray nodules, 4 to 6 mm. in diameter, of regenerating liver parenchyma. Near the center of the right lobe was a gray mass of tissue about 6 by 8 cm. with irregular prolongations which on surfaces made by cutting appeared as discrete nodules of tissue. One margin of this mass was beneath the liver capsule on the front surface. A dilated branch (4 by 2 cm.) of the portal vein adjacent to the tumor was filled with gray tissue 5.5 cm. long. Histologic preparations of the gray mass contained carcinoma tissue with an arrangement into papillary structures having a delicate fibrous stroma and suggesting an origin from duct epithelium. There was a pigment cirrhosis of the liver tissue itself. Deposits of brown pigment like those of the liver were present also in the pancreas, in the suprarenal glands and in the biliary lymph nodes. Hemofuchsin and hemosiderin granules were demonstrated in these tissues according to the method suggested by Mallory, Parker and Nye (*J. M. Research* **42**:461, 1921). A chemical analysis of 350 Gm. of liver tissue fixed in formalin failed to demonstrate copper. However, since the tissues had been kept in formalin for about a year before the chemical analysis was made, the copper compounds may have been dissolved.

While many details regarding the past history of this patient could not be obtained, it is known that he used alcohol excessively, and for over ten years had worked as a tradesman on metal lamps.

PHILADELPHIA PATHOLOGICAL SOCIETY

Regular Meeting, Feb. 10, 1927

EUGENE L. OPIE, *Presiding*

DEMODEX FOLLICULORUM IN NORMAL SKIN OF AXILLA. FRED D. WEIDMAN.

As far as I can discover, this observation is unique, in that the axilla was the part involved. This arachnid is a common commensal in the skin of the face, but is also on record as occurring on the breasts (Somerset and Chambers: Lancet **208**:172 [Jan. 24] 1925), scalp and eyelids.

The parasite has been described in connection with a variety of different dermatoses, more particularly cancer and acne rosacea, but molluscum contagiosum melanoderma, lichen spinulosus, blepharitis, impetigo contagiosa and alopecia areata have also been included. On the other hand, in a systematic examination of series of cases of alopecia, carcinoma, eczema, furunculosis, herpes, impetigo, lichen, lupus, pityriasis, etc., Gmeiner could not find demodex in the majority of cases, and when present the parasites were no more numerous than in the sound parts of the skin.

In addition to showing the parasite in the normal axillary skin, the presentor showed slides from another case in which the parasites were occurring in connection with a tremendous hyperplasia of the sebaceous glands; this material came from a lesion on the face of a man, aged 60, which was diagnosed clinically as epithelioma. It was stated that he did not have acne rosacea.

Histologically, there was no trace of carcinoma — the prominence of the lesion must have been referable to the tremendous hyperplasia of sebaceous glands (not adenomatous) and a heavy accumulation of keratinous material in the orifices of the hair follicles.

The significance of this parasite has been discounted generally by the numerous older observers who so carefully studied this mite. The consensus of opinion was that it was not the cause of any of the diseases enumerated, and that it was not a porter of leprosy, as contended by some. However, I would revive atten-

Demodex Folliculorum in Normal Skin of Axilla.

tion to this subject in view of the comparatively recent developments in regard to the experimental production of cancer with *Spiroptera neoplastic* by Fibiger.

BACILLUS LEPRAE IN SWEAT APPARATUS; HYGIENIC SIGNIFICANCE. FRED D. WEIDMAN.

I am indebted to Dr. Baldwin Lucke for these specimens of nonulcerated nodular leprosy. The point to the case is that the bacilli are clearly demonstrable both within the cells of the sweat glands and in their lumina. This finding stands out more prominently in view of Unna's pronouncement (Histopathology of the Skin, English translation by Sir Normal Walker, New York,

The Macmillan Company, 1896, p. 607). "In the coil glands we find no bacilli; but very often, in and around them, individual and clustered groups of those globules already described in connection with the neurolepride, which, like the bacilli, resist acid, and are evidently in some way connected with them."

The question of artefact, such as Unna disposes of in connection with the bacilli within blood vessels in his sections must also be dealt with in my sections. Thus, where there are such myriads of organisms present, it is inevitable that some should be lifted into the mounting medium and distributed nearby; actually, this has taken place to some extent in my sections. To establish the validity of my observation, there still remain, however, the following circumstances:

1. The bacilli are congregated definitely *within* sweat cells; furthermore, they are unassociated with other bacilli lying above the plane of the tissue.

Lepra bacilli in sweat glands.

2. The bacilli occur consistently within the lumina of the *same set of sweat coils,* as examined in different sections, whereas a different set of coils will show few or none.

They were present both as degenerate forms and as definite, well formed rods. The question may, of course, arise whether such examples are viable and capable of reproducing the disease; this, however, is much less of a problem than formerly, since so many instances are known in which the granular, apparently degnerative, forms of bacteria, streptothrices and spirochaetae have been demonstrated to have the capacity to reproduce disease.

The practical point of this observation is the probability of the bacilli reaching the surface of the skin in the absence of any ulcerative lesion. There are many who contend that subjects of leprosy should not be quarantined unless they have open lesions. I have always felt that such lesions may be present

in the nose without the patient or his medical attendants being aware of it, and in the sections exhibited there is further evidence that such cases may also be infectious from the cutaneous direction without there being any demonstrable open lesions.

HEART SHOWING INTERVENTRICULAR SEPTAL DEFECT WITH SLEROSIS AND ADHESION TO TRICUSPID VALVE LEAFLET. H. W. JONES and B. L. CRAWFORD.

The specimen was from a white woman, aged 49, who died from renal insufficiency following hysterectomy. In her history the only points of importance were that she had been a "blue baby"; that although she knew that a cardiac murmur existed, symptoms referable to the heart had not appeared throughout an active life.

On physical examination cyanosis, dyspnea or clubbing of the fingers was not evidenced. The only significant observation was a loud blowing, prolonged systolic murmur, most intense in the fifth left interspace 1.5 cm. to the left of the sternal border. It was present over the xyphoid cartilage and was transmitted to the aortic area, to the apex, and was also heard posteriorly below the angle of the right scapula.

At autopsy the heart weighed 270 Gm. The cusps of the tricuspid and mitral valves were definitely thickened and sclerosed. The aortic valve was normal. In the interventricular septum just beneath the base of the aortic cusps in the undefended space was a circumscribed fibrous nodule, about the center of which, on the left ventricular side, were two small depressions. Through one of these a small probe could be passed into the right ventricle, the opening being much smaller on the right side of the septum. One of the cusps of the tricuspid valve was adherent to the interventricular lesion.

A TUMOR OF THE MEDIASTINUM. C. J. BUCHER. (From the Department of Pathology, Jefferson Medical College and Hospital, Philadelphia.)

The specimen, a large mediastinal tumor, was removed at autopsy from a young woman, aged 20. The growth occupied the anterior mediastinum in the position of the thymus and completely surrounded the first portion and arch of the aorta, pulmonary artery, superior vena cava and pulmonary veins. It reached to the sternal notch above and below, and compressed the pericardial sac and its contents so that the long axis of the heart lay in a horizontal position. Anteriorly, it was attached to the sternum but did not infiltrate it; posteriorly, it compressed the trachea, main bronchi and esophagus, and laterally it compressed the left lung and infiltrated its hilum. The right lung showed slight compression. The tumor occurred as a solid mass. It was fairly soft, yellowish gray, opaque and glistening. The cut surface suggested division into lobules and showed a few areas of softening. The pleura, pericardium, heart, left lung and outer walls of the great vessels were invaded by the tumor while there were extensive metastases to the retroperitoneal lymph nodes and kidneys.

Histologically, the tumor was composed chiefly of small, round cells having a meager cytoplasm and round or oval nuclei. Some of the nuclei stained solidly, while others were vesicular and showed well developed nucleoli and chromatin arranged at the periphery of this structure. The solid staining nuclei were smaller than those which were vesicular. Mitotic figures were present but not abundant. The cytoplasm of many of these cells exhibited

an affinity for eosin. The cells were arranged in small nests separated by an extremely delicate fibrous tissue reticulum. The tumor was quite vascular, the vessels consisting chiefly of thin walled capillaries. Although many sections were studied nothing was found which could be construed as a Hassell's corpuscle. In the heart, almost the entire ventricular wall was replaced by tumor cells; while in the kidneys the tumor cells were seen surrounding tubules and glomeruli.

The patient's symptoms and physical signs were chiefly those of compression of important structures: dyspnea, cough, dysphagia, cyanosis, swelling at the root of the neck, face, left arm and hand and engorgement of the vessels of the head, neck and trunk. Pain was not felt. The blood picture was not distinctive of any pathologic condition save a moderate secondary anemia. The urine showed a small amount of albumin, a few hyaline casts and a few leukocytes, but never any blood, though it was examined frequently. The blood Wassermann reaction was negative. About one month elapsed between the onset of definite symptoms and the death of the patient.

In view of the location of the tumor, its gross and histologic characteristics and the observations of others, especially those of Shridde and Simmond, it was concluded that the tumor was malignant and should probably be classified among those of thymic origin.

THE OCCURRENCE OF MULTINUCLEATED GIANT CELLS IN ADENOCARCINOMA. S. W. MULHOLLAND.

In the study of giant cells, the occurrence in inflammatory tissue and in sarcoma has been extensively treated in the literature, but little has been written on giant cells in carcinoma and less of their occurrence in adenocarcinoma.

Ewing states that giant cells in sarcoma arise from hypertrophy of tumor cells, in many cases from cell fusion in poorly nourished areas, while in the epulis they represent fused endothelium surrounding foreign material; in other cases he thinks amitotic nuclear division may be responsible for many. Now one is led to wonder why such conditions cannot be encountered in the growth of all carcinoma.

A great many cases have been reported of pavement epithelial carcinomas of the skin with giant cells. Borst in his work on tumors mentions the occurrence of foreign body giant cells around cornified epithelial nests. Peterson has reported foreign body giant cells in a large series of skin carcinomas. Fischer reports the occurrence of giant cells in the tumor and metastasis of a squamous cell carcinoma, which he attributes to chemical irritation of the surrounding tissue by disintegration of carcinoma cells.

This certainty of the occurrence of giant cells in squamous celled tumors has led many to use the factor as a diagnostic feature when giant cells are found in an epithelial tumor. One writer states, "It is certain that in carcinoma giant cells occur only in solid pavement epithelial carcinoma and never in adenocarcinoma."

In the routine examination of a surgical tissue at the Philadelphia General Hospital the present slides first came into my hands. The history of the case is interesting.

On July 7, 1926, the patient, A. K., aged 30, was admitted, with a chief complaint of an "Abscessed Breast." The present illness began ten weeks before entrance when she noted a lump in the right breast. The mass was opened and drained. The breast did not heal.

The history revealed five pregnancies. Five months before presentation, she had given birth to a full term child. Delivery was normal.

Physical examination showed the upper quadrant of the right breast to be indurated, purplish and tender. Two sinuses of the previous incisions were noted. The lower half of the breast was soft. A second lump was noted at the second interspace near the sternum. The axillary glands were the size of a walnut.

One month after entrance, the breast and axillary glands were removed. A clinical diagnosis of chronic suppurative mastitis was made.

The specimen received at the pathologic laboratory showed essentially the picture given in the physical examination. The nipple was not involved. When cut across there was noted within the breast from 2 to 3 cm. below the surface, a cavity measuring from 2 to 4 cm. in diameter. This cavity communicated with the sinuses mentioned previously and was lined with light green necrotic material.

Sections from this specimen showed a varied picture. In the breast and glands one saw large areas that appeared to be spaces in which cells were floating. The cells were large luscious looking cells which had a pink granular or hazy cytoplasm, with a pale staining, and in many cases vacuolated nucleus. One noted that many of the cells were multinucleated, formed by the fusion of degenerating cells and also by active proliferation of the nuclei.

In other areas one saw cells that were not so loosely arranged, but tended to arrange themselves in cords. They were separated by a fine fibrillar type of connective tissue similar to that seen in most types of adenomatous tumors. The cells were markedly anaplastic and differed from those described before in that they were closely packed and polygonal or columnar in shape. An occasional acinus formation was seen.

So in this one sees a case of true adenomatous carcinoma in which the epithelial cells have taken on giant cell forms. That the malignant cell is capable of minor degrees of polymorphism is well recognized. The interchangeability of the acinus and the solid structure in adenocarcinoma is familiar to every one, so, too, the origin of a squamous celled carcinoma from columnar epithelium, but greater variations than these have not as a rule been considered possible.

I believe that one sees in this case the origin of cells from glandular epithelium, with a marked degree of polymorphism called forth because of the extreme malignancy of the tumor or because of some infection or chemical factor, so that one may say that multinucleated giant cells may occur in all carcinomas in which the polymorphic tendency is marked.

ACUTE HEMORRHAGIC INFLAMMATION OF THE SUPRARENALS: REPORT OF TWO CASES. WALTER FREEMAN, Washington, D. C.

Hemorrhage into the suprarenals is sometimes encountered in stillborn children and following severe burns. In these cases it is usually massive hemorrhage and is associated with thrombosis of the suprarenal veins. The two cases reported below showed a diffuse hemorrhagic infiltration without obvious thrombosis, and both occurred in general paralytic patients suffering from acute streptococcus infections. In the first case the streptococcus was cultivated from the gland, but in the second case, although the streptococcus was found in the heart blood, a profuse growth of *Bacillus coli* was all that was obtained from the gland. It seems probable that in this case there had first been a streptococcus invasion. In the first case in which both suprarenals

were completely involved, death occurred quickly, whereas in the second, where one gland was relatively in much better condition, the agonal period was prolonged.

REPORT OF CASES

CASE 1.—A colored man, aged 38, was admitted to St. Elizabeth's Hospital in November, 1925, suffering from dementia paralytica. Malaria inoculation on two occasions failed to excite the disease. Early in November, 1926, he developed furunculosis of the scalp. Three furuncles were opened, and on that day (November 8) and the next he was out of bed apparently feeling fairly well. On the evening of November 9 he suddenly became very weak, and on examination, when the intern arrived a few minutes later, he was found to be unconscious. The temperature had risen from 97 to 100.6 F., the pulse rate was 98, weak and thready; the respirations were 30, and there were râles at the bases of the lungs. The patient died at 10:15 p. m., less than an hour from the time he was noticed to be sick.

Necropsy, forty hours post mortem, revealed early interstitial lobular pneumonia, with fibrinous pleuritis and relatively inactive tuberculosis. The heart and brain showed clear signs of syphilis. The right suprarenal weighed 9.5 Gm., the left 11 Gm. On exposure, the tissue surrounding the glands on each side was found to be infiltrated by blood. The glands were swollen and firm, and showed hemorrhagic dots beneath the capsule. Section revealed marked hemorrhagic extravasation into the medulla of each organ, with invasion of the cortex from within outward. Sometimes this penetration had taken place in linear fashion between the columns of cells, sometimes there was massive eruption of the hemorrhagic mass through the cortex beneath the capsule. The tissue was not particularly soft. Hemorrhagic infiltration rather than massive hemorrhage was observed. Histologically, the vessels in the medulla were enormously distended with blood and ruptured in places, but they did not show any thrombi. In the medulla the blood cells appeared intact, but in the cortex they seemed to be laked, and much of the cortex was reduced to a homogeneous, pink stained mass with numerous small nuclei. Beneath the capsule were a few masses of relatively normal cortical cells. A pure culture of medium chain hemolytic streptococcus was obtained from the heart blood and from one of the glands.

CASE 2.—A man, aged 25, a mulatto, was admitted to St. Elizabeth's Hospital in April, 1925, suffering from dementia paralytica. An attempt at treatment by relapsing fever failed and he deteriorated progressively during his stay in the hospital. Early in January, 1927, he suffered cerebral concussion from a fall, and was treated by rest and local applications for a lacerated eyebrow. This wound became infected and progressed to orbital cellulitis with involvement of the eye and the development of metastatic cellulitis in the thigh. His condition did not improve after incision and drainage, and he tore the dressings from the wounds. The temperature remained subnormal most of the time and there was practically no leukocytic reaction in the blood. A rise in temperature to 103 F. heralded death, four days after surgical treatment of the eye and thigh.

Necropsy was performed twenty-three hours post mortem. There was spreading cellulitis of the orbit and thigh on the right side, with hemorrhagic inflammation of the lung and pleura. The brain was the seat of parenchymatous neurosyphilis. The right suprarenal weighed 10.2 Gm., the left 19.6 Gm. The latter had a thin capsule and a dark surface. Section disclosed a swollen turbid hemorrhagic cortex and medulla, with scarcely any distinction between

them. The architecture was practically undecipherable. It was diffuse hemorrhagic infiltration again, rather than massive hemorrhage. The right suprarenal was much less affected but it also showed areas of hemorrhage in both the cortex and the medulla. Histologically, the left organ showed massive hemorrhagic infiltration of the medulla, extending into the cortex between the columns of cells, but the blood appeared to be relatively fresh and not laked as in the first case. The cortical cells were plainly distinguishable although severely swollen and sometimes disintegrated. Culture of the organ yielded a heavy growth of *Bacillus coli.*

MINNESOTA PATHOLOGICAL SOCIETY

Regular Meeting, Feb. 15, 1927

GEORGE E. FAHR, M.D., *President,* and E. T. BELL, M.D., *Secretary*

A METHOD FOR TAKING REPEATED BLOOD PRESSURE READINGS IN LABORATORY ANIMALS. LEONE MCGREGOR.

Investigators attempting to produce chronic arterial hypertension experimentally find it necessary to take a long series of blood pressure readings on each animal. With the method of a cannula in an artery only a few readings are possible. These may be influenced by the anesthesia and operative measures employed. Three bloodless methods for taking blood pressure in animals have been published.

1. Hilding Anderson (Demonstration of an Instrument for Taking Repeated Blood Pressures in Rabbits with Report of Some Experiments, Proc. Exper. Biol. & Med. **20**:295, 1925) took readings in the central artery of a rabbit's ear with a special instrument which he devised for the purpose. When heat radiation is controlled, this method seems to be satisfactory. However, if a large artery can be used, there is less danger of vasomotor changes affecting the result.

2. Theodore Fahr (Verhandl. d. deutsch. path. Gesellsch., 1912, p. 234) applied the ordinary blood pressure cuff around the abdomen of the rabbit and read the pressure when the femoral pulse disappeared. This is a difficult method to apply because the femoral pulse is not easy to hear or feel.

3. Frederick Allen (Auscultatory Estimation of Blood Pressure of Dogs, J. Metab. Research **4**:431, 1923) put the blood pressure cuff around the dog's thigh with the phonendoscope inside the lower border and over the course of the femoral artery. This is not satisfactory on the rabbit.

My method is a combination of the procedures used by Fahr and Allen. The rabbit is tied in the dorsal position. The phonendoscope is applied over the termination of the abdominal aorta, where it may be held in place by tapes. The cuff is wound around the lower part of the abdomen just above the iliac crests so that the phonendoscope is just inside the lower border. As Allen has pointed out, the sounds are more clearly heard when the phonendoscope is under the cuff than when it is distal to it as in clinical procedures.

The readings are taken in the usual manner. The cuff is inflated until the aortic pulse disappears. Then the mercury is allowed to fall. The first sound which comes through is taken as the systolic pressure. With a further fall in the mercury, the sound becomes softer. This is taken as the diastolic pressure.

The aortic sounds are sharp and distinct, and the pressure can be read as accurately as in man. The normal aortic systolic pressure in rabbits varies from 115 to 140 mm. of mercury. Epinephrine shows the same sharp rise which occurs when the pressure is measured with a cannula in the carotid. The blood pressure can be read as accurately in monkeys as in rabbits.

A Method of Producing Experimental Chronic Hypertension in the Rabbit. A. H. Pedersen.

The kidney is approached by the posterior route. A longitudinal incision is made about 1½ inches to the left of the mid-dorsal line, and the lumbodorsal fascia is exposed. Following the line of cleavage and separating the muscles in the direction of their fibers, the perirenal space is entered. The kidney is pushed out with a little gentle pressure on the abdomen. The fatty capsule is stripped off and the renal vein and artery are identified and separated. An aluminum wire band is placed around the renal vein, and sufficiently constricted so that the kidney becomes tense and purplish. The whole kidney is placed in a loose pouch of fixed animal membrane to prevent the development of collateral circulation. The opening is surrounded by a purse string suture drawn about the renal pelvis and vessels. The kidney is then replaced, and the wound sutured in layers.

In the five rabbits which have survived the operation for two weeks or more, there has been a definite elevation of the aortic blood pressure, from 110 to 130 (normal) to 180 mm. of mercury or higher. The highest pressure recorded was 270 mm. of mercury. The blood pressures were read by Dr. Leone McGregor by the method she has just demonstrated to you. One rabbit which has survived the operation for fifty days has a blood pressure of 180 mm of mercury.

It is suggested that the hypertension is of reflex origin, due to increased resistance in the circulation through the obstructed kidney.

Henoch's Purpura with Report of a Case. Donald McCarthy.

A man, aged 43, in October, 1926, had a purpuric eruption around the knee joints and ankles, with fever and abdominal pain. On admission one week later, there was a purpuric eruption around the knee and ankle joints, pain in the joints, generalized abdominal tenderness, vomiting and fever. The vomitus contained microscopic blood. There were bloody stools continuously and many erythrocytes in the urine. The temperature varied from 100 to 102 F.; the pulse rate was 100. The platelet count was 223,000; there was no low platelet count at any time. The bleeding and clotting times were normal. The capillary resistance test was normal. The hemoglobin content was 70 per cent; there were 4,000,000 erythrocytes, 11,000 white cells and 75 per cent polymorphonuclears. The spleen was not enlarged.

In brief, the patient presented a picture of acute multiple arthritis with abdominal pain and blood in the vomitus and feces, with a purpuric eruption. There was no evidence of a primary purpura, since the bleeding time was normal and the capillary resistance test normal. This seems to correspond closely to what is described in the literature as Henoch's purpura.

At the present time (four months after the onset of the illness) the symptoms have largely cleared up. The patient still has a little pain in the left shoulder, and from time to time small purpuric spots appear on the feet and disappear later.

ELECTROCARDIOGRAPHIC OBSERVATIONS IN DIPHTHERIA HEART. M. H. NATHANSON.

There is still considerable uncertainty as to the exact mechanism of the circulatory failure in diphtheria. Most pathologists agree that the myocardium shows extensive degenerative changes. Grossly, one finds cloudiness and softening of the muscle. Microscopically, there is seen a varying amount of hyaline necrosis of the muscle, sometimes with an increase of fat. In cases which terminate with acute dilatation of the heart there is extensive necrosis of the myocardium. There are many observers, however, who believe that the pathologic conditions in the heart do not offer convincing evidence of the cause of death.

The myocardial changes in diphtheria were studied in a series of cases by means of the string galvanometer. Electrocardiographic tracings were made of fifteen cases of diphtheria during convalescence. In eight cases the disease had been of a severe type, and of these, seven showed inversion of the T wave in one or more significant leads. In two cases sudden death occurred, while in the remaining five subsequent tracings showed a return to an upright T. On an average, the electrocardiogram became normal about eight weeks after the onset of the illness. Most patients with the T inversion did not show any other clinical evidence of myocardial involvement. It is suggested that the patient, following diphtheria, be kept under extreme restriction until the electrocardiogram becomes normal. With the exceptions of alterations in the T, changes were not noted.

Seven cats were given sublethal injections of diphtheria toxin. In six of these, electrocardiographic tracings showed inversion or flattening of the T wave corresponding to clinical diphtheria. There was also a tendency for return to normal.

At the present time inversion of the T wave has not been noted in other forms of toxic myocardium.

Book Reviews

THE SIGNIFICANCE OF THE PHYSICAL CONSTITUTION IN MENTAL DISEASE. By F. I. WERTHEIMER and FLORENCE E. HESKETH, with a preface by LEWELLYS F. BARKER. Pp. 76, ten chapters. Price, $2.50. Baltimore: Williams & Wilkins Company, 1926.

The authors, in the words of Dr. Barker, "have undertaken an examination of mental patients from the standpoint of external habitus, with the idea of testing the contemporarily popular hypothesis that physical habitus and mental reaction types exhibit a more or less definite correlativity," and the work is to be welcomed, "as an American contribution to an important movement in medicine that lays stress on the *human individual*, or the *person*, as such, aside from the 'health' that he enjoys or the 'disease' that may account for his inadequacy of responsivity when he is 'sick'."

The volume deals with the following items: Early studies of body types; beginning of medical anthropometric studies; anthropometric studies in psychiatry; heredity and constitution; comparison of classifications of morphologic types; observational and anthropometric methods in general; the material of this study; procedure of investigation; description of morphologic types used; methods of observation and description; body types found from observation; anthropometric methods; method of correlating observation types with one index; "constitutional indices"; weight; a new anthropometric index; characteristic "types" at ends of frequency curve; analysis of the components of the index; averages of some other anthropologic data; factors influencing morphologic habitus: (1) race, (2) age and growth and (3) occupation; correlation of psychoses and prepsychotic personalities with index values and body types from observation; conclusion; aspects of the human constitution; summary. A useful bibliography is added.

The main interest centers naturally in the validity and mode of recognition of the given "morphological types," and in the usefulness of anthropometry for their demarcation.

The types are three in number, and are defined as follows: 1. The "pyknic" person "has in profile a round head, the contour of the occiput, top of the skull and profile line impressing one often as a more or less clear circle. The outline of the head is soft without any sharply prominent parts (like nose or chin). The face has the form of a pentagon or a shield or in many cases a form between the two. It is always definitely broad and soft, quite apart from the fact that it is usually fleshy, especially as regards the nose. There can be no doubt that in the general aspect of the face the impression of a certain harmoniousness and balance is also conveyed by certain physiognomical-psychological characteristics which evidently may be a source of error. The neck is short and full, with the head set a little forward on smoothly rounded shoulders. The line from the tip of the chin to the suprasternal notch is characteristic, inasmuch as it tends to be not an angle but a smoothly sloping or even a straight line. The hair line usually borders the forehead in a regular unindented curve. Apparently the pyknic type has a tendency to baldness, and when this occurs it seems to be electively regular in outline and with a smooth shiny surface. The trunk is thick set and appears barrel-shaped, with the chest broadening toward the lower part of the body. One might say that the body cavities (head, chest, abdomen) tend to a voluminous

development. The limbs are relatively short, as are also the hands. The panniculus adiposus is well developed and the color of the skin is good. The pyknic habitus is most definitely pronounced in early middle age.

2. "The athletic type is characterized by a strong development of the locomotor apparatus so that the bones and muscles stand out in plastic relief. The heavy development of the skeleton is most easily recognized in the clavicles. The neck is strong and the trapezious muscles typically very well developed. The shoulders are large and the trunk tapers down from the broad shoulder girdle to the relatively narrow pelvis, so that the trunk outline from the front can be schematically designed as a trapezoid. The limbs are relatively long, the hands and feet are large and the fingers often of a blunt, thick and 'acromegaloid' character. The hair is abundant and the hair line tends to grow in a peak in the center of the forehead, receding in bay-like manner on either side toward the temples. The face has a long egg form. A line which would connect the upper forehead, tip of nose, and chin would be a gentle curve.

3. "The asthenic habitus is characterized by the general impression of a deficiency in volume combined with an average unlessened length, so that these individuals impress one as being taller than they really are. The thorax is long and flat and the shoulders narrow, and the trunk can be schematically described as cylindrical. The legs and arms are long and thin with lean muscles. The face is of short egg form and may show hypoplasia in varying degree. The skin tends to be pale, thin, and with but scant fat. The profile is usually markedly irregular. The line which would connect upper forehead, tip of nose and chin tends to be angular on account of the disproportion between the long nose (which seems sharp on account of lack of fatty upholstering) and the small mandible. When the hypoplasia of the jaw is not so marked there may be noted simply a long nosed profile. The neck is thin and seems elongated. The body hair is scanty and these individuals may also tend to baldness, but with an irregular outline and a more or less wrinkled surface."

As help in the determination of these types the authors give the following new anthropometric index:

$$\text{"Index} = \frac{\text{Leg length} \times 10^5}{(\text{Transverse chest D}) \times (\text{sagittal chest D} \times (\text{trunk height})} \times 100$$

D represents diameter.

"This index is based on de Giovanni's conception that the impression of the existence of morphological types is based on the relation of trunk volume to limb length. In the 65 patients of this study the observation types agree remarkably with the index values, showing that the extreme low index values correspond to the pyknic type and the extreme high values to the asthenic type, with the less characteristic types between. In this way it is shown for the first time with exact anthropometric methods that there are no types in the strict sense, but only transitions which probably fit into a normal frequency curve, the extreme forms impressing one as types."

Pages 70 to 72 are given to a summary of the observations, etc., which is followed by the bibliography and by a number of plates illustrating the defined types.

It is evident that the authors have made an earnest and intelligent effort, much above some others in this line, at a separation and definition of certain physiologic and structural types, and at their significance in relation to disease, more particularly to pathologic conditions in the brain. Unfortunately the subject is so complex that the success of this as well as that of all previous efforts

in this direction is but limited and full of uncertainties in application. The main obstacle lies in the difficulty of eliminating the evolutionary and racial together with the numerous individual and nonphysiologic variations. Round or long head, shorter or longer neck, normal lankness or robustness of the body, etc., are commonly group characteristics with but little and that only incidental relation to disease. Anthropometry may indeed be of use to psychiatry and other branches of medicine, but only on the amplest and sound basis of studies on the general population.

There are "constitutions," as there are "temperaments"; but they occur in such an infinity of gradations and mixtures that all effort to pin them down to something simple and practical is disappointing.

A. HRDLIČKA.

TUBERCULOSIS, BACTERIOLOGY, PATHOLOGY AND LABORATORY DIAGNOSIS, WITH SECTIONS ON IMMUNOLOGY, EPIDEMIOLOGY, PROPHYLAXIS AND EXPERIMENTAL THERAPY. By EDWARD R. BALDWIN, M.D., Director of the Trudeau Foundation, S. A. PETROFF, PH.D., Bacteriologist and Director of Trudeau Sanatorium Research and Clinical Laboratory, and LEROY S. GARDNER, M.D., Pathologist and Director of Saranac Laboratory for the Study of Tuberculosis. Pp. 342, with 82 engravings and 4 colored plates. Price, $4.50. Philadelphia: Lea & Febiger, 1927.

Ever since Trudeau's pioneer researches in tuberculosis and since — after the destruction by fire of his improvised laboratory — he performed what Osler termed the "Phoenix trick," his institution at Saranac Lake has been a prominent center for active investigative work. The authors of the present volume have been exponents of these activities; thus, their publication of a monograph on the pathology, bacteriology and laboratory diagnosis of tuberculosis meets with more than the usual amount of interest. The title of the book invites comparison with I. Straus' classic work along similar lines, or, perhaps, with Calmette's book, which is an attempt to bring Straus' treatise up to date. It is evident, however, that the present monograph serves different aims. It represents a brief discussion of the subjects mentioned, based chiefly on the experiences, and, it should be emphasized, on the opinions of the authors, with little consideration of literature. Such a richness of individual experience renders this book an unusually reliable guide for physician and technician in actual laboratory procedures, because in addition to the mere recipes, the intricacies and stumbling blocks of the routine technic are well discussed. Diagnostic tests which are not as fully established in value, as for example the demonstration and culture of tubercle bacilli, are, with the exception of Petroff's method of complement fixation, too casually mentioned. The laboratory worker would undoubtedly be interested to learn more than is offered here about some of the recently advocated methods, such as nonspecific serum flocculations, sedimentation reaction, Abderhalden's reaction and other forms of complement fixation (particularly since the methods of Calmette and Massol, Besredka, and Nègre and Boquet are more widely in use than the one explained in detail). The very briefness of this discussion constitutes here what must be considered as misstatements. For example, the statement "The more rapid rate of sedimentation indicates active disease when compared with a normal control blood," without further qualification, is obviously misleading. The pronouncement made in connection with complement fixation," it has been definitely proved, that only tubercle bacilli, or their derivatives can act as antigens in this reaction," appears not justified, since a number of investigators had very fair results with antigens prepared from other acid-fast bacilli, and Seiffert with extracts

from beeswax. It comes rather as a surprise that it is stated here, "that antigens are lipoprotein in nature," disregarding completely Zinsser's recent work on the carbohydrates in this rôle, work in which one of the authors has been actively associated. In the more theoretical parts of the book a fuller statement of controversial points in regard to significant problems, such as Much's granules and the filtrable forms of tubercle bacilli for example, would have been desirable. It is felt that the careful conservatism which is an outstanding mark in this work, interfered to some extent with a more extensive discussion of problematical points which would have added interest; this applies, for example, to the competent discussion on the histogenesis of tubercle, based almost exclusively on the recent work of American investigators. The theory of primary pulmonary infection is accepted with only slight discussion of the intestinal theory and without mention of Allen K. Krause's views at all. In the chapters on human pathology Ghon's and Ranke's concept of the primary complex are adopted, but Ranke's most significant studies on the relation of tissue allergy to the propagation of the disease in the secondary and tertiary stage are not referred to. Instead, a concept of the development of pulmonary phthisis is presented which appears to be an addition to the already too variegated classifications of the disease. The strictly localized apical lesions are named secondary stage, and the frankly progressive processes disseminating from these through the lungs are presented as tertiary stage. The differentiation into proliferative and exudative lesions according to Aschoff's teaching is introduced, relating the latter, however, to the allergic condition of the host.

In a modern guide on the laboratory science in tuberculosis a grammatically and scientifically more felicitous nomenclature than the one used in the bacteriologic table ("B. butter," "B. turtle") might be expected. One should like to see an occasional error corrected, such as stating the optimal p_H for the growth of tubercle bacilli as 7.0, whereas recent work by Schaade and Claussen showed that it is on the acid side, coinciding thus with the p_H of acute tuberculous exudates. The avian type of tubercle bacillus is reported as nonpathogenic for pigs, though a large percentage of tuberculosis in this animal is caused by the avian type. Similarly, this type is definitely pathogenic for cows, at least during pregnancy. In the list of tuberculins Omnadin is included, although it is not, and has never been, claimed to be a derivative of tubercle bacilli; partial antigens are prepared by dissolving bacilli not in lecithin, as stated, but in lactic acid.

Nevertheless, this criticism will not detract from the fact that in addition to the topics already mentioned, experimental infection, reinfection, immunity, predisposition, epidemiology and prophylaxis are reliably discussed, the essentials always being assembled with admirable briefness. The book is recommended as a source of initial information.

STUDIES ON TSUTSUGAMUSHI DISEASE. By RINYA KAWAMURA, M.D., Professor of Pathology, Niigata Medical College, Niigata, Japan. Authorized English translation edited by N. C. Foot, M.D., and Shiro Tashiro, Ph.D., Dr. Med. Sc. (Hon., Kioto). Price, $3. Pp. 229, 25 half-tone plates, with numerous charts and figures. Published as Nos. 1 and 2, Vol. IV, The Medical Bulletin, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

The author, well known through his publications on lipoid infiltrations, has been investigating tsutsugamushi disease (Japanese flood fever) since 1913 and, therefore, writes with the authority of long experience. As the malady is

unfamiliar to the average American physician, this book is valuable both as an authoritative source of reference and as something of a novelty in medical literature. So far as I know, it is the only complete volume on this subject, the literature on flood fever being scattered through a score of monographs and articles over a period of some thirty-five years.

Beginning with an introductory historical survey, Kawamura takes up the clinical aspects of the disease (with several typical case reports), its pathology in man and experimental animals, the etiology (which remains obscure), the entomology and ecology of the vector (*Trombicula akamushi,* Brumpt, a minute mite of the "red-bug" or acarid family) and, in conclusion, an interesting description of the methods devised for the prevention of the development and transmission of the disease. A bibliography of 186 references, together with twenty-five half-tone plates of photographs, photomicrographs and drawings, comprising seventy-four figures, completes the book.

Trained in the German school of pathology, Kawamura approaches his subject with meticulous thoroughness, omitting nothing and covering every aspect of the disease with painstaking detail. If one were to criticize his work it would be to suggest that the summaries of the various chapters are too full and tend to repeat too much of the subject matter that precedes them, and that some of the minutiae incidental to the experimental and other protocols should be taken for granted, rather than included in the text.

The sections on the comparative entomology and the prevention of the disease are particularly well done and interesting; the halftone illustrations are excellent and adequately serve their purpose in supplementing the text. The arrangement of the subject matter is logical. The book should be particularly valuable to physicians in northwestern Japan and in Korea where the disease is endemic.

PHYSIOLOGY AND BIOCHEMISTRY IN MODERN MEDICINE. By J. J. MACLEOD, Professor of Physiology in the University of Toronto, Toronto, Canada, assisted by Roy G. Pearce, A. C. Redfield, N. B. Taylor, J. M. D. Olmsted and others. Ed. 5, with 291 illustrations, including 9 plates in color. Price, $11. St. Louis: C. V. Mosby Company, 1926.

This textbook has survived the inclusion of the bold adjective "modern" in its title through four successful editions. Its especial field is the application of the principles of chemistry and physics to the phenomena of life in such a way that the knowledge can be used by physicians. The present, completely revised edition has been especially expanded in the sections on the neuromuscular system and on the physiology of the special senses in order to be available as a textbook of physiology for advanced students in medicine.

The book is divided into ten parts: the physicochemical basis of physiologic processes, the blood and lymph, the neuromuscular system, the special senses, the circulation of the blood, respiration, digestion, excretion of urine, metabolism and the ductless glands. The chapters on carbohydrate metabolism and the demonstration and functions of "insulin" are especially interesting.

It is remarkable how much some of the newer material has gained in tangibility and coherence through separation from the context of the original articles. The consecutive sections, although necessarily brief in a volume of such scope, are presented in such a way as continually to invite ideas of clinical application. One wonders if the utilization of much new scientific information does not wait on its inclusion and correlation with older information in an authoritative, stimulating presentation such as this.

Books Received

EDUARD R. V. HOFFMANN'S LEHRBUCH DER GERICHTLICHEN MEDIZIN MIT GLEICHMÄSSIGER BERÜCKSICHTIGUNG DER DEUTSCHEN UND ÖSTERREICHISCHEN GESETZGEBUNG. Elfte auflage. Vollständig umgearbeitet von Dr. Albin Haberda, o. ö. Professor der gerichtlichen Medizin in Wien. Mit neuer Bearbeitung des psychiatrischen Teiles von Dr. Julius Wagner-Jauregg, o. ö. Professor der Psychiatrie in Wien. Pp. 1294. Price, 57 marks in paper cover. Berlin and Vienna: Urban & Schwarzenberg, 1927.

EXAMINATION OF CHILDREN BY CLINICAL AND LABORATORY METHODS. By ABRAHAM LEVINSON, M.D., Associate in pediatrics, Northwestern University Medical School. Ed. 2. With eighty-five illustrations. Pp. 192. Price, $3.50. St. Louis: C. V. Mosby Company, 1927.

STUDIES FROM THE INSTITUTE FOR MEDICAL RESEARCH KUALA LUMPUR FEDERATED MALAY STATES No. 20. Notes on Malayan Culicidae by A. T. Stanton, M.D., F.R.C.P., D.P.H. Pp. 94. London: John Bale, Sons & Danielson, Ltd.

ANNUAL REPORT (reprinted papers) OF THE INVESTIGATIONS CARRIED OUT UNDER THE SUPERVISION OF THE THERAPEUTIC RESEARCH COMMITTEE OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION, Volume XV, 1926.

HISTORY OF THE MAYO CLINIC. Sketch of the History of the Mayo Clinic and the Mayo Foundation. Octavo volume. Pp. 185, illustrated. Cloth. Price, $3.50 net. Philadelphia and London: W. B. Saunders Company, 1926.

PHYSICIANS OF THE MAYO CLINIC AND MAYO FOUNDATION. Physicians of the Mayo Clinic and Mayo Foundation. A series of 635 biographical sketches with 611 portraits and including complete and accurate data concerning the professional life of each physician prior to Jan. 1, 1926. Octavo volume. Pp. 578. Cloth. Price, $7. Philadelphia and London: W. B. Saunders Company, 1927.

THE CLINICAL INTERPRETATION OF BLOOD CHEMISTRY. By ROBERT A. KILDUFFE, director. Laboratories, Atlantic City Hospital. Pp. 186. Price, $2.50. Philadelphia: Lea & Febiger, 1927.

CHILD LIFE INVESTIGATIONS. Social Conditions and Acute Rheumatism. Special Report Series, 114, Medical Research Council. Pp. 108. Price, 2s. 6d. London, 1927.

HISTORY OF CARDIOLOGY. By Louis Faugeres Bishop, M.D., and John Neilson, Jr., M.D. With an introduction by Victor Robinson, M.D. Pp. 71. Price, $5. New York: Medical Life Press, 1927.

DIE BIOLOGIE DER PERSON. Ein Handbuch der allgemeinen und speziellen Konstitutionslehre unter Mitarbeit zahlreicher Fachmänner herausgegeben von Prof. Dr. Th. Brugsch und Prof. Dr. F. H. Lewy. Vol. 1 (Lieferungen 1-3). Price, 55.80 marks, in paper covers. Berlin and Vienna: Urban & Schwarzenberg, 1927.

THE HARVEY LECTURES 1925-1926. Delivered under the Auspices of the Harvey Society of New York. Series XXI. By F. R. Nager, Some Recent Otological Problems. John H. Northrup, Dynamics of Pepsin and Trypsin. Warren H. Lewis, Transformation of Mononuclear Cells. Edwin B. Wilson, Empiricism and Rationalism. Knud Faber, Historical Outline of Medical Therapy. B. Brouwer, Comparative Anatomy and Neuropathology. J. B. Collip, Parathyroid Glands. Pp. 229. Price, $4. Baltimore: Williams and Wilkins, 1927.

THE NEWBORN, PHYSIOLOGY AND CARE. By CLIFFORD G. GRULEE, M.D., LL.D., clinical professor of pediatrics, Rush Medical College of University of Chicago, and Barnet E. Bonar, M.D., Salt Lake City, Utah. Pp. 258, 63 illustrations. New York and London: D. Appleton & Co., 1926.

THE NEWBORN, DISEASES AND ABNORMALTIES. By CLIFFORD G. GRULEE, M.D., LL.D., clinical professor of pediatrics, Rush Medical College of University of Chicago, and Barnet E. Bonar, M.D., Salt Lake City, Utah. Pp. 429, 82 illustrations. New York and London: D. Appleton & Co., 1926.